| 40 | I P K E O K Y I P K D O K Y I P E G O R Y T - H G R G - | D 90 | N E P L Y | 0 I F K 0 T Y O O I L K O T Y Y O T Y Y Y Y Y Y Y Y Y | 190 | - K E G S C G F F K E G S C C A F F K E G S C C A F F F S C A F F F F F F F F F F F F F F F F F F |
|------|---|--|----------------------|--|-------|---|
| 30 | A I D T Y Q E F E E A Y A I D T Y Q E F E E T Y A A D T Y K E F E R A Y S S E M F S E F D K R Y | 80 1 R S L L Q S W 1 L R S L L L E S W | 13 | M G R L E D G S P R T G M G R L E D G S R R T G M R E L E D G S P R A G E L I V S O V H P E T K | F 180 | V E T F L R I V O C R S V E T F L R M V O C R S A E T F L R W M K C R R I D N Y L K L L K C R I |
| 20 A | LRAHRLHOLLIOAHRAHOL LRAGHHOL VLSHYIHNL | 70 E T O O K S N L E | 0 A Q Q M N Q K D | D L E E G I O T L D L E E G I O T L D L E E G I O A L O T K R L L E G M | 170 | Y C F R K D M D K S C F R K D M D K H C L R R D S H K |
| 10 | - L S R L F D N A H - L S R L F D H A M - L S S L F A N A V | 60 C E S I P I P S N R E D S I P T P S N R E | S L A T P E D K | S D S N Y Y D L L K S D S D D Y H L L K S D - R V Y E K L K I L S K A V E I E E | 160 | L K N Y G L L K N Y G L L L K N Y G L L L S A Y Y N L L L L L L L L L L L L L L L L L |
| _ | V 0 1 V P | B 50 S F L Q N P Q T S L C F S S F L H D S Q T S F C F S | FITKA-INSCH D 100 | - R S V F A N S L V Y G A - R S M F A N N L V Y D T - S R V F T N S L V F G T V T E V R G M O E A P E A | 150 | S K F D T N S H N D D A L S K F D T N S H N H D A L D K F D T N L R S D D A L W S G L P S L Q M A D E E |
| | hGH hPL pGH [| hGH hPL | hPRL | hGH hPL pGH hPRL | • | hGH hPL pGH hPRL |

FIG. — 2

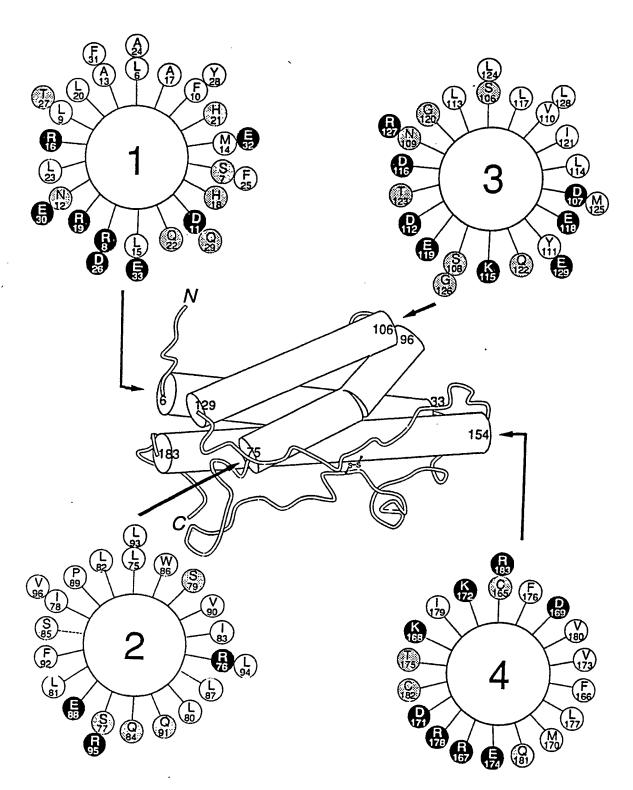
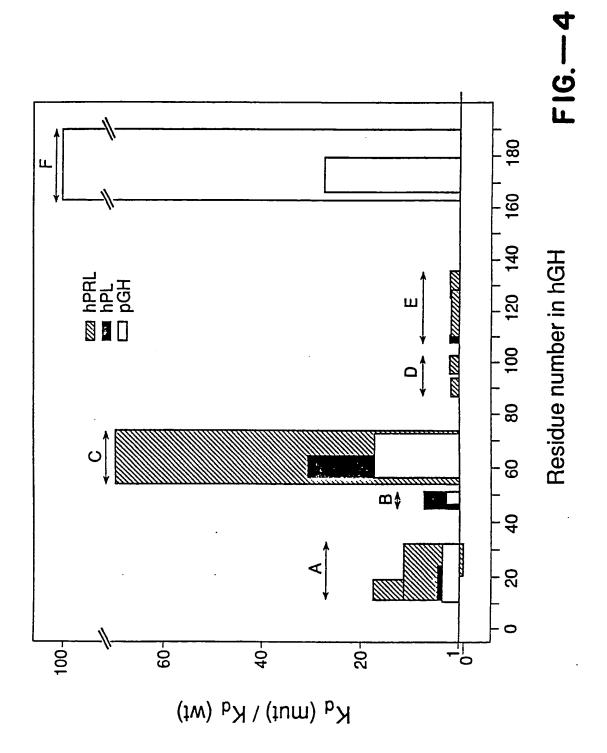
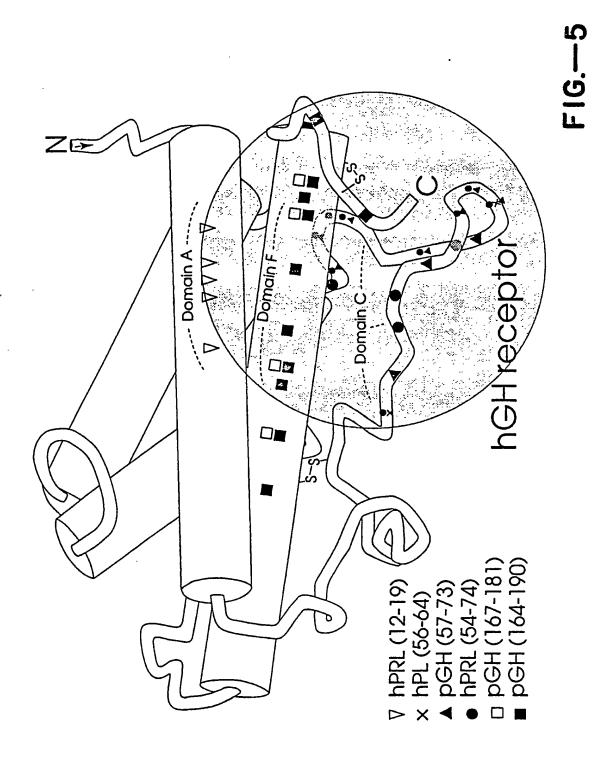


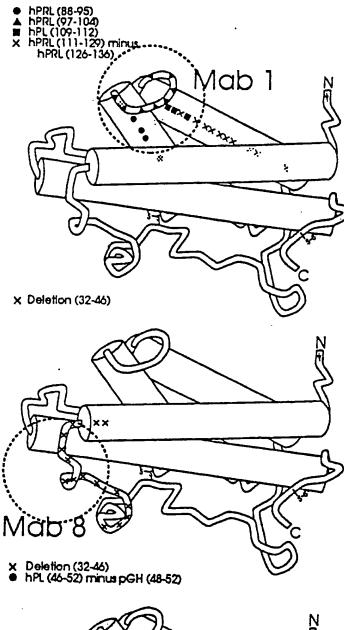
FIG.—3



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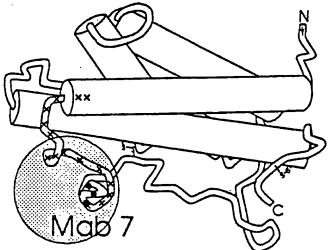
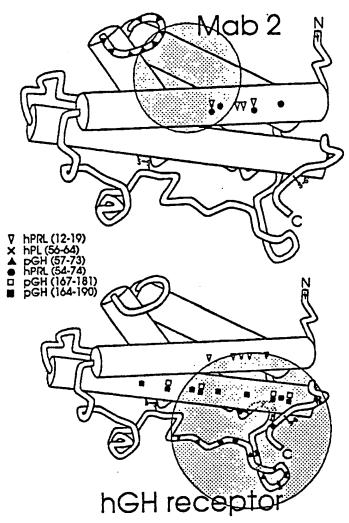


FIG.-6A

pGH (11-33) minus hPRL (22-33)
 hPRL (12-19) minus hPL (12-25)
 hPRL (97-104)



pGH (57-73) minus hPRL (54-74)
 pGH (164-190) minus pGH (167-181)

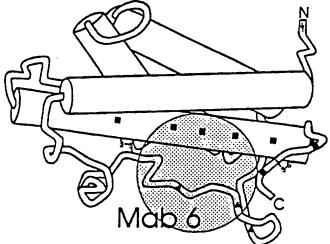
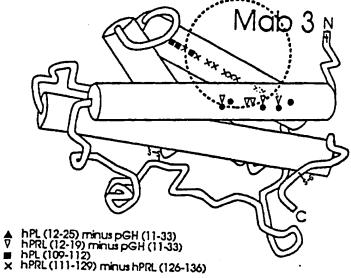
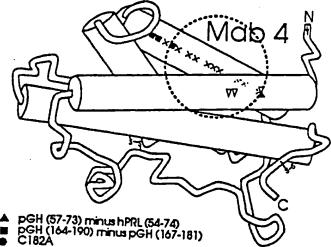


FIG.-6B

- pGH (11-33) minus hPRL (22-33) ▲ hPL (12-25) minus hPRL (22-33) ▼ hPRL (12-79) hPL (109-112) ★ hPRL (111-129) minus hPRL (126-136)





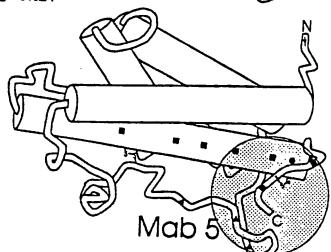
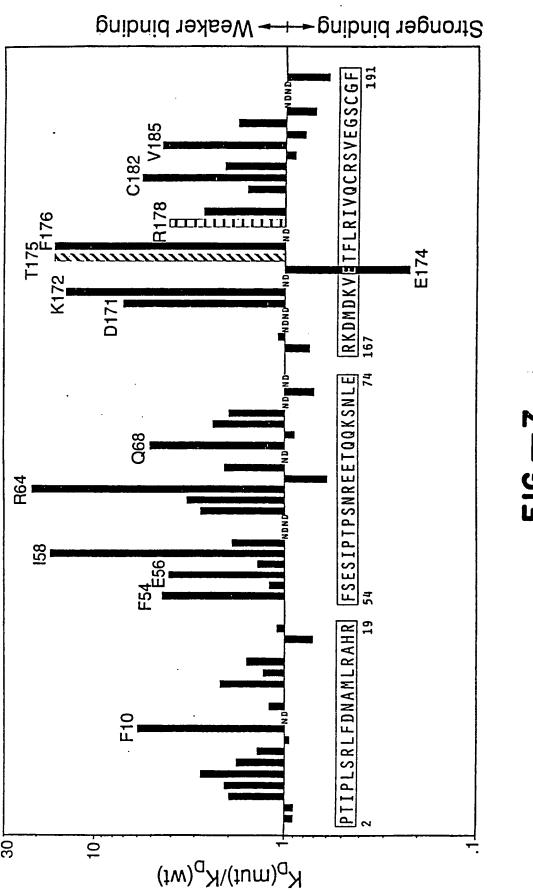


FIG.-6C



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| | | | | | 20 1y GG BamHi | | | |
| Ala GCA | Ala GCC | Pro | Asn | Val GTC | 120 G1y GGG Bar | Ser | Lys Aag | am* Tag |
| Tyr Ala TAT GCA Nsii | n Leu G CTA Nhei | Asn | Ser | Ser AGT | Glu GAA | Tyr Tac | Arg AGG | Phe TTC |
| Ala GCC | Gln Leu CAG CTA NheI | Leu Gln CTG CAG PstI | 70 Lys AAA | Arg Agg | Glu GAG | The | Phe | 190 G1y GGC |
| Asn AAT | His | Leu (CTG (PstI | Gln | Leu CTG | Leu CTA | Gln CAG | Cys TGC | Cys TGT |
| Thr Aca | 20 Leu CTT | Phe TTC | Gln | Phe 1 TTC (| Asp Gac | 140 Lys AAG | Tyr TAC | Gly Ser GGC AGC Pwil |
| Ala GCT | Arg | Ser | Thr | Gln | Lys AAG | Phe TTC | Leu | 614 667 P4 |
| Ile ATT | His | Tyr Tat | Glu | 90 Val GTG | Leu CTG | Gln Ile CAG ATC Bglii | Leu CTG | Glu GAG |
| Ser | Arg Ala CGG GCC ApaI | 40 Glu Gln Lys GAA CAG AAG | Glu GAG | Pro | Leu CrG | Gln CAG Bg1 | G1y GGG | Val GTG |
| Phe TTT | Arg Al CGG GC Apal | 40 Gln CAG | Asn Arg AAT CGC | Leu Glu CTC GAG (XhoI | Asp GAC | G17 GGG | 160 Tyr TAC | Ser |
| Val | Leu CIT | Glu GAA | Asn AAT Ny | Leu CTC Xho] | TYF | Thr | Asn | Arg |
| Phe TTC | Met ATG | Lys Aag | Ser | Trp 166 | 110 Val GTG | Arg CGG | Lys AAG | Cys TGC |
| Met ATG | Ala GCT | Pro | Pro | Ser | Asn | Pro Arg CCG CGG | Leu | Gln |
| Ser | Asn | Ile | 60 Thr ACA | Gln CAG | Asp Ser GAT TCG AsuII | Ser AGC | Leu CTA | 180 Val GTG |
| Ala GCA | Asp Gat | TYF TAT | Pro | Ile | ASP GAT AS | 61y 660 | Ala GCA | Ile |
| Leu | 10 Phe TTC | Glu Ala GAG GCC StuI | Ile Att | Leu CTC | Ser TCT | 130 Asp Gat | Asp Gac | Leu Arg CTG CGC MstI |
| Leu | Leu CTA | Glu A] GAG GC StuI | Ser TCG | Leu CTG | Gly Ala GGC GCC Nari | Glu GAA | Asp Gat | Leu CTG Mst |
| Phe TTT | Ser Arg AGT CGA Sall | Glu GAA | Glu Ser GAA TCG | BO Ile Ser Leu ATA AGC TTG Hindili | GLY GGC Nari | Leu | Asn | Phe TTC |
| -Ala GCA | Ser AGT Sa | Phe TTT | Ser TCA | Ser AGC LndII | TYF | Arg Agg | His | Thr |
| Ile | Leu CTA | 30 Glu GAG | Phe | Ile ATA H | Val GTC | G1y GGG | 150 Ser TCA | Glu GAG |
| Asn | Pro | Gln CAG | Cys TGT | Arg CGC | Leu CTG | Met ATG | Asn AAC | val Grc |
| Lys Asn AAG AAT | Ile ATA | Tyr | Leu | Leu CTC | 100 Ser AGC | Leu Met CTG ATG | Thr Asn ACA AAC | Lys Aag |
| Lys Aaa | Thr | Thr | Ser | Glu Leu GAG CTC SacI | Asn | Thr | Asp Gac | Asp GAC |
| Met | Pro | Asp GAC | 50 Thr ACC | Glu] GAG (SacI | Ala GCC | Gln | Phe TTC | 170 Met ATG |
| | +1 Phe TTC | Phe TTT | Gln CAG | Leu CTA | Phe TTC | Ile | Lys | Asp |
| - | 79 | 142 | 214 | 286 | 358 | 430 | 502 | 574 |

FIG.-9

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| alui hindili 1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTTATTT AAGCTTTGGA GATTATCGTC ACTGCAATGC CITAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTCTG TACTTTTAG AGTAACGACT CAACAATAAA TTCGAAACCT CTAATAGCAG TGACGTTACG | sau3AI hinPI hinPI hhai hhai hlai l TICGCAATAT GACCAACAGC GGTIGATTGA TCAGGTAGA GCCCGCTGT ACGAGGTAAA GCCCGATGCC AGCATTCCTG ACGACGATAC | thai haeili smaili thudhi hai-] foki mnli alui eagi bbvi hinPi saaBi sfani storcececcacacacacacacacacacacacacacacacaca | hphi 1 Tatagtogot ttgttttat tttttaatgt attigtaact agtacgcaag ttcacgtaaa aagggtatct agaggtigag gtgatttt atg aaa 2 Ataicagcga aacaarta aaaaattaca taaacattga tcatgcgttc aagtgcattt ttcccataga tctccaactc cactaaaa tac ttt 3 Met Lys | bsmI nsil 5 AAG AAT ATC GCA TTT CTT GCA TCT ATG TTC GTT TTT TCT ATT GCT ACA AAT GCC TAT GCA TTC CCA ACT ATA CCA CTA TTC TTA TAG CGT AAA GAA GAA TAC AAG CAA AAA AGA TAA CGA TGT TTA CGG ATA CGT AAG GGT TGA TAT GGT GAT 1 Lys Asn Ile Ala Phe Leu Leu Ala Ser Met Phe Val Phe Ser Ile Ala Thr Asn Ala Tyr Ala Phe Pro Thr Ile Pro Leu | taq! sau96[[M.haeIII-] asu1 sau91 sau96[[M.haeIII-]] nlaili taq! hindli taq! hindli taq! hindli taq! ban11[[M.haeIII-]] asu1 hindli taq! hindli taq! asu1 mboli alui bstNI ear! haeI correct Granger G |
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| | - द सम | tagi xhoi paeR7i avai[M.taqi-] CTC GAG | | ០០១ | un a | מו ל ל ב"ל |
| | aqi AC TG | | . u | CTG | | AAG TTC |
| CT a | F Pro | H H H H H H H H H H H H H H H H H H H | econi bspMI | CTG | | AGG TCC Arg |
| เ | infi tac ATT TAP | TCG AGC Ser | a d | GAC CTG | oii (c dam- dam- rrc AAG | TTC AAG Phe |
| caqılm.cıaı | FI P P P P P P P P P P P P P P P P P P P | srI CAG GTC | saI | TAC ATG TYF | mboll [dam-] sau3Al mbol [dam-] dpnl tholl satYl satYl satYl c ATC TTC c TAG AAG | TGC ACG Cys |
| (| PIGPE BIGER | 0 (1)(0 (1) | _ 4 | GTG CAC Val | Sagasti | TAC ATG TYF |
| | leI TCA AGT Ser | I fokI CIC ATC GAG TAC | . tag | AAC TTG Asn | 666 617 617 | r CTC GAG Leu |
| | TT | fnu4HI bbvI rg CTG rc GAC | stBI suII fi[M | TCG AGC Ser | | fnu4HI bbvI G CTG C GAC |
| | TGT ACA Cys | I £ II b TTG AAC Leu | bstBI asuII hinfI[M.taqI- I-] taqI | GAT CTA ASP | | 901 |
| | nli CTC GAG Leu | alu indI AGC TCG Ser | . hha | LI TCT AGA Ser | thal fuud bstU sacii CCG C GGC G | TAC ATG TYF |
| | mnli mnli ACC TCC CT TGG AGG GA Thr Ser Le | -] alui fnu hindili bbv C ATA AGC TTG C G TAT TCG AAC G | hinPI hhaI laIV arI giCI aeII anI | acyl mnll GGC GCC TCT GA1 CCG CGG AGA CT? Gly Ala Ser Asp | fnu4HI bbvi GC AGC CG TCG | AAC TTG Asn |
| | 4 H H | I-] luI- CGC GCG | hind hhar nlarv nari haici haeii bani | 864 666 614 614 | 000 | AAG TTC Lys |
| | CAG GTC Gln | saci mnli hgidii hgidii bspl286[M.alui-] banii[M.alui-] GAG CTC CTC CGC 7 CTC GAG GAG GCG 7 | | AG FG | | CTC GAG Leu |
| | AC CCC TG GGG Sn Pro | T MI | [dcm | DSTNI ACCI GC CTG GTC TC CG GAC CAG A er Leu Val T | mboli GAA G CTT C | CTA GAT Leu |
| • | 4H4 0 | sacr sacr hgid hgid bapi GAG CTC | CrFI | Star CTG GAC Leu | CTG GAC Leu | r GCA CGT Ala |
| | CAG GTC GLD | CTA GAT Leu | w d. | ă Ĥ ŭ | mnli G AGG C TCC Y Arg | hgal GAC CTG ASP |
| | pstI CTG GAC | AAC TTG | | DSTXI CC AAC GG TTG la Asn | 950 | GAT CTA ASP |
| | TTC AAG Phe | TCC | • | SO A | ATG TAC Met | AAC TTG Asn |
| | r TCA A AGT | AAA TTT | į | mboli GTC TTC CAG AAG Val Phe | CTG | CAC GTG His |
| | TAT ATA TYr | CAG GTC GIn | i | | ACG TGC | TCA |
| | S AAG C TTC | CAA F GTT | | AGT TCA | dam- CAA GTT | AAC |
| | A CAG r GTC n GIn | A ACA I TGT | mnli i li | AGG TCC | ~ C C C L . S | ACA TGT |
| | G GAA CTT G Glu | LI C GAA C CTT | mn. dder mstir ecosii | ESG3 | | taqi TC GAC AG CTG |
| | CVI S.A.A.G TIC | DDII IDII IUI mul GAG CTC | | TIC Phe | I GAA CTT | FL of TP |
| | Styl CCC 3 GGG T | thar fnuDIJ bstUI nruI mr I CGC GG | | CRC TI | mnlI GAG CTC Glu | AAG TTC Lys |
| | ATC TAC II | AA TT S.S. | | GTG CAC Val | I PI CTA GAT GAT Leu | AGC TCG Ser |
| | TAT ATA TYE | mnll CC TCC GG AGG | JII 1286 | GAG CCC CTC GGG Glu Pro | sau96I avaII asuI ppuMI eco0109I mr AAG GAC CTA GZ TTC CTG GAT CT | TAC ATG TYr |
| | 000 000 1 % 1 % | 065 | ligi. | | P P P P P P P P P P P P P P P P P P P | ACC TGG Thr |
| | 557 | 639 61 | | 719 | 800 | 881 |
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| | dcm- | | | |
| aluI Sa | IV ecoRII CI bstNI I hphI CACCGTCACC | nheI fnu4HI bbvI GGCGTGCTGC | 11 CTCGCTAACG GAGCGATTGC | CCGCCATCTC |
| 14HI I al CTGCCCA GACGGGT | | , , , , , , , , , , | | _ 50 50 50 50 50 50 50 50 50 50 50 50 50 5 |
| 5 2 4 | nlaIV hgiCI lI banI rCGG CA(| CTAT | nlaIV hgiCI nu4HI banI CGGCAC | hgaI thaI fnuDII bstUI CGCGT |
| TA AH | nla hgi mnli foki ban TCATCCTCGG | rI CAGTCACTAT GTCAGTGATA | nlaIV hgiCI fnu4HI mspI banI hpaII mre CCGCCGCAC | hgaI thaI fnuDI bstUI TCCATCGCGT |
| C TIC G AAG Y Phe | _ | bsrI G CA | fnu fnu mspI hpaII haeI hg CCGCC | |
| H1-) T GGC T CGG | : CATC | ANI | IGGAA | VACAT |
| alui Tuli[A.H. 14HI AGC TGT TCG ACA Ser Cys | hinPI hhaI GCGCTCATCG CGCGAGTAGC | sfani bsri ACAGCATCGC CAGTCACTAT TGTCGTAGCG GTCAGTGATA | l nlaIV hgiCI fnu4HI mspI banI hpaII mn naeI TGAATGGAG CCGCGGCAC | GCAGAACATA CGTCTTGTAT |
| alui pvuII[M.H1-] fnu4HI [bbvI GGC AGC TGT GG CCG TCG ACA CC Gly Ser Cys Gl | | | 1 | |
| mnli GAG G CTC C | ATCTAACAAT TAGATTGTTA | GTCCATTCCG | II I[M.haeIII· taqI mnli CACCTCGACC GTGGAGCTGG | styI pflMI CCAACCCTTG GGTTGGGAAC |
| GTG CCAC CAL | | | haeIII au96I[N I I II III SuI n III n III c | |
| TCT (| ATGA. TACT | I-] ecoRV Gatat | scrFI ncil mspi hpali V asu ccali | hinPI stI spI hhaI GCGCAA |
| 14HI CGC GCG Arg | CGTGTATGAA GCACATACTT | haeIII sau96I[M.haeIII-] asu1 FI I I II II II II mnll ecoRV GGGCCTCTT GCGGGATATC | i e Si | hinPI mstl fspl bsml hhai GAGAACTGTG AATGCGCAAA |
| H∢U | | M.h HT AA | | bsi GTG 7 CAC 1 |
| CAG GTC Gln | nlaIV hgiCI banI AGTCAGGCAC TCAGTCCGTG | haelli sau961[M.] asul rrfi sil spl sall null mnll cGGCCTCTT | | b: Gagaactgtg Ctcttgacac |
| GTG CAC | | しょうりょうけいじ | | |
| fani I I S ATC 3 TAG 4 Ile | AACGC | al ms ht ccc racrec | I hgaI TGCGT ACGCA | etecc Pacco |
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| hi hb mst fst fst fst fst fst fst fst fst | | | | |
| CA GT hr | msel Cacagilaaa Gigicaatit | CIIGGITAIG | mnli TCTGCCTCCAGGGGGGGGGGGGGGGGGGGGGGGGGGGGG | nlaiv GGAGCCAATC CCTCGGTTAG |
| ត ពី ភូបិដ | | | | |
| taqi GIC GI Val G | TTAT | TAGG | CTTG | I SAATT |
| | GGTAGTITAT CCAICARATA | TAGGCATAGG | CTATACCTTG | PflMJ -} CCAAC GGTTC |
| tthl GAC CTG | | | | hphr TG AC |
| aIII ATG TAC Met | nseI GCTTTAATGC CGAAATTACG | sfani foki CTGGATGCTG GACCTACGAC | fnu4HI hinPI hhaI haeII TAGCGCCGC | hphI pflMI hinfi[M.hphl~) GATTCACCAC TCCAAGAATT CTAAGTGGTG AGGTTCTTAA |
| SCT | | | | |
| 962 | 1041 | 1141 | 1241 | 1341 |

FIG.- 100

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|--|--|--|--|--|--|
| | GGGT | mboli GTCT | GTGG | NACGT | TTAC |
| | CTGGCGGGGT GACCGCCCCA | IIII TGAATGGTCT ACTTACCAGA | TACCCTGTGG | mnli GTTGTTTACC CTCACAACGT CAACAAATGG GAGTGTTGCA | TCCCCTTAC |
| | | nlaiii NACA TGA FTGT ACT | | mnli FACC CTC ATGG GAC | |
| scrfl ncil caull sau961 nlalv avall asul mspl | 091 CCCGGCTAGG GGCCGAICC | nle AGCAACAACA TCGTTGTTGT | fnu4HI NI bbvI TGCTGCTGGC | FEGTT AACAA | II GAACAGAAAT CITGICTITA |
| sauger casauger nlarv avari assui m | ⊣ | - н | fnu4 sfaNI fokI bbvI GGA TGCTG | | |
| <u> </u> | ecoo. mnli TCGTTGAGGA AGCAACTCCT | dde: creccaccre Gacccrecac | m-] : : ani fok CATCGCAGGA GTAGCGTCCT | bsr] CATACCGCCA GTATGGCGGT | nlal TTACCCCCAT AATGGGGGTA |
| | | | sau3AI mboi[dam-] dpni hoii stYi lwi ii sfaNi II II II CATCTG CAT | | |
| hgiAI I | msti mbol(dam-) fspi dpni bsp1286 TGCGCATGAT CGTGCTCCTG ACGCGTACTA GCACGAGGAC | fnu4HI bbvI fnu4HI bbvI CGACTGC TGCAAAACGT GCTGACGACG | sau3AI mbol[dam-] dpnI xholI bstYI alwI hpalI bspMII scolII sfaNI fokl bbvI TCCGATCTG CATCGCAGGA AGGCCTAGAC GTAGCGTCCT | I fokI sfaNI fnu4HI CCGCCGCATC | ATCGGTATCA TAGCCATAGT |
| 33 | mbol(dam-) dpnl bsp12 IGAT CGTGC1 CTA GCACGP | fnu4HI bbvi 14HI igc rgc | | ω> ⊔ | |
| nla I | m dp CATGA | fnu bbv fnu4HI bbvI cGACTGCTGC GCTGACG | ACCATTATGT TGGTAATACA | sau96 nlaIV avaII asuI TTCTCGGTC AAGAGACCAG | CTCTCGTTTC GAGAGCAAG |
| nl hinPI | | | | | LI CTCI |
| cm-] | ball[dcm-] I[dcm-] TGGCCACGGG ACCGGTGCCC | GAACGTGAAG CTTGCACTTC | hinPI hhaI haeII AGCGCCTGC TCGCGGGACG | ddel GCATTGACCC TGAGTGATTT CGTAACTGGG ACTCACTAAA | mnli foki sfaNi TGAGCATCCT (|
| haeIII haeI scrfi[dcm-] ecoRII bstNI 961[dcm-] II [dcm-] I eaeI I cfrI | bali 91 (dc TGGC ACCG | | | ddel C TGAG G ACTC | |
| hael hael scrFI[dc ecoRII bstNI sau96[dcm- avaII[dcm- avaII[dcm- | nlaIV ball[do eco01091[dcm-] GGGICC IGGCCAC CCCAGG ACCGGIG | thai fnuDII bstVI CGCGAGC GCGCTCG | I AAGTC TTCAG | d GACCC CTGGG | TATCG |
| <u>.</u> | GII | 140 | thaI fnuDII bstUI CGGGGAAGTC GCGCCTTCAG | GCATT | ACCCGTATCG TGGGCATAGC |
| | = | ohr I [M.hp NGCG | | hinPI hhaI haeII NAGCGCTG | CAGTA |
| | fnuDII aval fnu4) bstUI sfaNI bbvI acGGGGGGA TCTCGGGCAG TGCGCCGCGT AGAGCCCGTC | hinfi[M.hphi TGAATCACCG AT ACTTAGTGGC TA | AGTCTGGAAA TCAGACCTIT | h CGAA GCTT | ATCATCAGIA TAGTAGICAT |
| hinpi hhai HHI | sfaN CGCA GCGT | AGAA | | msel TTAA | IX III GTTC |
| hin hha fnu4HI | fnuDII bstVI sfaN accccccca rcccccccr | GITAGCAGAA | TGTTTCGTAA ACAAAGCATT | mseI TCTGTATTAA AGACATAATT | FI I nspcix III nlaIII GGGCATGTTC CCCGTACAGG |
| fnu4HI | | | | ACA T | scrfi ncil mspl r hpall caull ACC GGC |
| r. | fnu4HI bbvI CAGCAGCCGC GTCGTCGCCG | bsrI TGCCTTACTG ACGGAATGAC | TCGGTTTCCG | AACACCTACA TTGTGGATGT | scr nci msp hpa bsrI cau TCCAGTAACC |
| | 1441 | 1 + 5 : . F + 1 + 5 : . | 1641 | 1741 8 | 1841 7 |
| | | | | | |

FIG.—IOD

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| msel TTAACGCTTC TGGAGAACT CAACGAGCTG AATTGCGAAG ACCTCTTGA GTTGCTCGAC | <pre>mspl[%.bamHI-] hpail spMil cclii 3AI I[dam-] I[dam-] I I I I CC GGAAATTGTA AACGTTAAAA GG CCTTTAACAT TTGCAATTT</pre> | AAATCAAAAG AATAGACCGA GATAGGGTTG TTTAGTTTTC TTATCTGGCT CTATCCCAAC | sau961[M.haelII-] haelii asul draili CCGTCTATCA GGCCTATGC CCACTACGTG GGCAGATAGT CCCGATACCG GGTGATGCAC | 11 286 hpair 1 alui naei CCCCCGATTT AGAGCTTGAC GGGGGAAAGCC GGGGGTAAA TCTCGAACTG CCCTTTCGG |
|---|--|--|---|---|
| AAGCCAGACA TTCGGTCTGT | b sau sau dhu dhu dhu dhu dhu dhu dhu dhu dhu dh | AATCCCTTAT TTAGGGAATA | GGGCGAAAAA CCCGCTTTTT | hgiJ bspl banI nlalv CTAAAGGGAG GATTTCCCTC |
| sau961[M.haeIII-] haeIII asuI III GGCCC GCTTTATCAG CCGGG CGAAATAGTC | aluI TGAGCTTTAC | I HANTCGGCAA TTTAGCCGTT | CAACGTCAAA GTTGCAGTTT | nlaiv AATCGGAACC |
| sau963 haeIII asuI mseI nlaIII AACCGCCCTT AACATGGCCC TTGGCGGGAA TTGTACCGGG | ACCACGCIGA | haeIII CAATAGGCCG GTTATCCGGC | pleI hinfI ACGTGGACTC | TAAAGCACTA |
| | I fi TCGCTTCACG | msel ATTTTTAAC TAAAAATTG | mseI CTATTAAAGA GATAATTTCT | nlaIV hgiCI mnli taqI banI iT CGAGGTGCCG |
| AACAGGAAAA TTGTCCTTTT | xmnI hinfI CATCTGTGAA T | eI AAATCAGCTC TTTAGTCGAG | pleI hinfI CAAGAGTCCA GTTCTCAGGT | TTTTGGGG |
| I CAAGTGACCA GTTCACTGGT | thai fnubli bstul hgai foki GACGCGGATG AACAGGCAGA | I msel AATTTTGTE A | bsrI AGTGTTGTTC CAGTTTGGAA TCACAACAAG GTCAAACCTT | CIAATCAAGT |
| sfaNI mnli ACGGAGGCAT C TGCCTCCGTA G | | msel thal fnuDII bstUI .ATTCGCGTTA | bsrI 2241 AGTGTTGTTC CAGTTTGGAA TCACAACAAG GTCAAACCTT | hphi 2341 AACCATCACC CTAATCAAGT TTGGTAGTGG GATTAGTTCA |
| 1941 | 2041 | 2141 | 2241 | 2341 |

FIG.—10E

| | 7 | 1/50 | | |
|--|--|--|---|--|
| thai fnuDII bstUI[M.hha fnu4HI CCGGC | | | 4 5 | S. P. C. P. C. P. C. P. P. C. P. |
| ACAC | bsmaI GAGACGGTCA | T I AGTCACGTAG TCAGTGCATC | NI TGCGTAAGGA ACGCATTCCT | CAAAGGCGGT GTTTCCGCCA |
| thai fnubii bstUi[M.hhai-] inPi hai hai C GCGTAACCAC C | scrFl u4HI mspl vI nciI cauII aluI hpal | bsr tthill nlaili CATGACCC GTACTGGG | sfani ACCGCACAGA TG TGGCGTGTCT AC | aluI TCAGCTCACT AGTCGAGTGA |
| thaI fnuDII bstUI(hinPI hhaI fnu4HI bbvI GTCACGCTGC GCGT | fn bb nlalii nspCix TCTGACACAT GC | fnu4HI bbvI hinPI hhaI TCGGGCGCA GC | GGTGTGAAAT AG | GAGCGGTA |
| AAGTGTAGCG TTCACATCGC | hphI mn) GGTGAAAACC CCACTITIGG | TTGGCGGGTG | hgiai bsp1286 apali ndei AGTG CACCATATGC | fnu4HI fnu4HI bbvI TTCGCTGCG GC AAGCCGACGC CG |
| hinPI hhai haeii GGGCGCTGGC | L.hhaI-] haI-] haI-] hphI CGGTGATGAC | hgaI thaI fnuDII bstUI[M.hhaI-] inPI haI CGCG TCAGCGGGTG | ddeI tI ACTGAGI TGACTCI | hinPI fnu4HI pleI bbvI hinfI hhaI TGACTCGCTG CGCTCG |
| hinPI hhai haeII GCGGCGCTA CGCCCGCAT | thar thar fuuDII bstUI[M.hhaI- I-) hinPI thar fuuDII bstUI[M.hhaI-] mnlI hhar CC TCGCGCGTT CGGTGGGGG AGCCACG | h TCAGG AGTCCC | rsal AGCAGATIGI AO TCGTCTAACA T | |
| AGCGAAAGGA TCGCITTCCT | Ida [M. amH | GACAAGCCCG | sfaNI fnu4HI GCGGCATCAG | mnll CCTCGCTCAC GGAGCGAGTG |
| mboll AAGGGAAGAA TTCCCTTCTT | sau3) mboi dpni alwi xhoi nlaiv bspMii hgal bamHi thai mspi[M.ba bstUl[M.bai] hinpi hpail hhai acciii hhai acciii cccccccccccccccccccccccccccccc | scrfi ncil mspi hpali vi cauli GCCGGGAGCA | mseI GCTTAACTAT CGAATTGATA | eari pi I mboli C TCTTCCGCTT |
| GCGAGAAGG | msel fnu4HI hinPI hinPI hhaI hhaI GCGCTTAATG CGCGGCTACA | sfani foki GTAAGCGGAT G | bsri acci GTGTATACTG CACATATGAC | hin hha faNI haeI CATCAGGCG GTAGTCCGC |
| GGCGAACGIG | | aluI CAGCTTGTCT GTCGAACAGA | CGATAGCGGA GCTATCGCCT | sl GAAAATACCG CTTTTATGGC |
| 2441 | 2541 | 2641 | 2741 | 2841 |

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| | | | , 0 | /33 | | |
|---|---|--|--|---|--|---|
| II I GTTGCTGGCG CAACGACCGC | scrFI[dcm-] ecoRII bstNI C CAGGCGTTTC G GTCCGCAAG | alui TTTCTCAIAG AAAGAGTAIC | mspi hpaii CTTATCCGGT GAATAGGCCA | GGCGGTGCTA CCGCCACGAT | AAAGAGTTGG TTTCTCAACC | sau3AI mbol[dam-] alwi xholi bstYi mboll[dam-] AGAAGATCCT TCTTCTAGGA |
| thal fnuDII bstUI fnu4HI haeIII AAAAGGCGG GT | sc ec bs ATAAAGATAC TATTTCTATG | hinPI haeII AGCGTGGCGC TCGCACCGCG | hinPI hhai fnu4HI bbvI ACCGTGGGG CT | mnli GAGGTATGTA GC CTCCATACAT CC | ACCTTCGGAA AA TGGAAGCCTT TI | sau3AI mbol[dam—dpnI xhoII bstYI alwI AAGGATCTCA A |
| FI[dcm-] SRII INI II NABACCGTA TCCTTGGCAT | CC CGACAGGACT | T CCCTTCGGGA | C GITCAGCCCG | A TTAGCAGAGC T AATCGTCTCG | bsrI T GAAGCCAGTT A CTTCGGTCAA | hinPI hhaI thaI HI fnuDII bstU[M.hhaI-] GCAGATACG CGCAGAAAA |
| I hae GCAAAAGG CGTTTTCC | mnli GAGG TGGCGAAACC | GT CCGCCTTTCT CA GGCGGAAAGA | hgiai bsp1286 apali GTGCA CGAACCCCC | srI CT GGTAACAGGA GA CCATIGTCCT | hinPI hhaI CT GCGCTCTGCT GA CGCGAGACGA | HI : :GCAGATTA CGTCTAAT |
| h CAAAA GTTTT | AAGTCA TTCAGI | mspi hpaii ACC GGATACCTGT IGG CCTATGGACA | GCTGT | fnu4HI bbvI alwNI I bbvI bsrI 3GC AGCAGCACT | STA TTTGGTATCT | TTTGCAA |
| nlaIII nspCIX AAAG AACAIGTGAG TTTC TIGIACACTC | hgar taqi AAAA ATCGACGCTC TTTT TAGCTGCGAG | mspI fnu4HI hpaII ccr gccgcrracc gga | aluI ccc rccaacrics ccc accricacc | fnt bbr bsrI TRT CGCCACTGGC | ACTAG AAGGACAGTA HGATC TTCCTGTCAT | GCGGT GGTTTTTTG |
| BATAA CGCAGGAAAG TATT GCGTCCTTTC | sfani KGGAG CATCACAAAA KGCTC GTAGTGTTTT | CCTG TICCGACCCT | TGTA GGTCGTTCGC | AAGA CACGACTTAT | GCTAC | TGGTA |
| hinfi TCCACAGAAT CAGGGGATAA AGGIGTCTTA GTCCCCTATT | nlaly GGCTCCGCC CCCTGACGAG CCGAGGGGG GGGAUTGCTC | hinPI II hhaI TCGTG CGCTCT AGCAC GCGAGA | ddel AGGIATCICA GTTCGGIGIA TCCATAGAGT CAAGCCACAT | mspI hpaII scrFI I nciI fI cauII ICCAA CCCGGTAGA | haelli hael CAAGIGGIGG CCTAACTACG CTICACCACC GGATTGAIGC | I -) CAAAC AAACCACGG STTTG TTTGGTGGCG |
| AATACGGTTA TCCAC TTATGCCAAT AGGTG | nlalv TTTTCCATA GGCTC AAAAAGGTAT CCGAG | scrFI[dcm-] ecoRII bstNI aluI mnlI hhaI CCCCTGGAAG CTCCCTCGTG CGCTCTCCTG | CTCACGCTGT AGGIA GAGTGCGACA TCCAT | pler hinfi AACTATGGTC TTGAGTCGAA TTGATAGCAG AACTCAGGTT | CAGAGTICTI GAAGI GICTCAAGAA CIICA | mspI hpali sau3AI mbol[dam-] dpnI aluI alwI TAGCTCTTGA TCCGGCAAAC |
| 2941 AATA | 3041 TTTT | 3141 CCCC | 3241 CTCA | 3341 AACT | 3441 CAGA(| aluI 3541 TAGCT |

| | | | 19/55 | • | |
|--|---|---|--|---|---|
| -) sau3AI mbol[dam-] dpnI alwI mseI xhoII draI bstYI ahaIII TAGATCCTTT ATCTAGGAAA | sau3AI mbol[dam-] ddel dpnl rcrcAGCGAT AGAGTCGCTA | -) thaI fnuDII bstUI AATGATACCG ITACIATGCC | foki mnli bsri GCCTCCATCC CGGAGGIAGG | TGTCACGCTC | mnll sau96I avall asul CTTCGGTCCT GAAGCCAGGA |
| mboll[dam-sau]AI mbol[dam-] dpnI xholl bstYI alwI hphI G GATCTTCACC I, | nlalv hgici bani mnli GAGGCACCTA | sau961[M.haeIII- nlaIV fnu4HI asuI bsrI bbvI GGCC CCAGIGCIGC | AACTITATCC TIGAAATAGG | pst[[M.Hl-] fnu4HI bbvI sfaNI GCTGCA GGCATCGTGG CGACGT CCGTAGCACC | alur GGGTTAGCTC |
| TATCAAAAA ATAGITITT | mseI G CTTAATCAGT C GAATTAGTCA | CCATCT | -] sau96I avaII asuI A GTGGTCCTGC T CACCAGGACG | CATT | G TGCAAAAAG C ACGTTTTTT |
| nlaiii bsphi G GTCATGAGAT C CAGTACTCTA | A GTTACCAATG T CAATGGTTAC | mnli G GGAGGCTTA | haelli sau961[M.haelli-] asul hinpl aelli-] hhal CCCGG CTCGCGAAA | I .A ACGITGITGC | sau3AI mboi[dam-] dpni alwi III nlaIII GATC CCCCATGTTG |
| msel ACTCACGITA AGGGATITIG TGAGIGCAAT TCCCTAAAAC | T TGGTCTGACA | AA CTACGATACG IT GATGCTATGC | prical part of the property of | hinPI hhai L msti fspi AT AGTTIGCGCA | nla TTACAT AATGTA |
| | ra tgagtaaact nt actcattiga | TC GTGTAGATAA AG CACATCTATT | | msel bsrI TC GCCAGTTAAT AG CGGTCAATTA | saulai mbol[dam-] dpni TTCCCAACGA TCAAGGCGAG |
| I FG TGGAACGAAA TC ACCTTGCTTT | CT AAAGTATATA SA TTTCATATAT | pleI hinfI IG ACTCCCGTC AC TGAGGGGCAG | IA TCAGCAATAA AT AGTCGITATT | AG TAAGTAGTTC IC ATTCATCAAG | ⊢ 6 |
| ddeI hgaI IC TGACGCTCAG | msel dral ahaIII TTT AAATCAATCT | P) hi CA TAGTTGCCTG | mspi hpali hphi nlalv GCTCACCGC TCCAGATTTA | scrfi ncii mspi hpaii cauli alui cccc GAAGCTAGAG | aluI TCAGCT |
| nm-] T CTACGGGGTC | ATGAAGT TACTICA | foki T CGTICATCCA A GCAAGTAGGT | | TTGTTG | T ATGGCTTCAT |
| saulai mboi[dam-] dpni 1 TTGATCTTTT C | mseI I TAAATTAAAA ATTTAATTTT | 1 CIGICIAITE GACAGAIAAA | bsmaI 1 CGAGACCCAC GCTCTGGGTG | mseI aseI 1 AGICTATTAA TCAGATAATT | 1 GTCGTTTGGT CAGCAAACCA |
| 3641 | 3741 | 3841 | 3941 | 4641 | 4141 |

FIG. - IOH

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| 20/55 |

| | | 20/5 | 3 | |
|--|---|--|---|--|
| foki bbvi GGCAGCACTG CATAATTCIC TTACTGTCAT GCCATCCGTA AGATGCTTTT CCGTCGTGAC GTATTAAGAG AATGACAGTA CGGTAGGCAT TCTACGAAAA | ahaII[M.hpaII-] acyl mspI hpaII hpaII scrFI hindII thaI cauII hgaI CGACCGAGTT GCTCTTGCC GGCGTCAACA CGGGGTAATA GGCGCCACA | bsrI sau3AI sau3AI mboI[dam-] dpnI xhoII alwI AACTCTCAAG GATCTTAGGAT GGTCAAGCTA CATTGGGTGA TTGAGAGTTC CTAGAATGGC GACAACTCTA GGTCAAGCTA CATTGGGTGA bsrI bsrI bsrI taqI bsrI caqI bsrYI bs | fnu4HI ACAGGAAGGC AAAATGCCGC AAAAAAGGGA ATAAGGGCGA TGTCCTTCCG TTTTACGGCG TTTTTCCCT TATTCCCGCT | nlaili bsphi bsmai Attiatcagg Gttattgict Catgagcgga tacatatttg aatgtattta Taaatagtcc Caataacaga Gtactcgcct atgtataaac ttacataaat |
| fn nlaiii bb TCAIGGITAI GGC | fnu4HI GTGTATGCGG CGACCGAGTT CACATACGCC GCTGGCTCAA | GGGGCGAA AACT | hphi GCGTTTCTGG GTGAGCAAA CGCAAAGACC CACTCGTTTT | TTATTGAAGC ATT AATAACTTCG TAA |
| GTGTTATCAC TO | ddeI TCTGAGAATA AGACTCTTAT | msel dral hgial ahali bsp1206 TAGCAGAACT TTAAAAGTGC TCATCATTGG AAAACGTTCT TCGGGGCGAA ATCGTCTTGA AATTTTCACG AGTAGTAACC TTTTGCAAGA AGCCCGGTT | hphi ACTTTCACCA TGAAAGTGGT | SSPI TTTTTCAATA AAAAAGTTAT |
| fnu4HI haeIII eaeI cfrI A GTGGCGCA T CAACCGGCGT | ACCAAGTCAT TGGTTCAGTA | AI 1286 xm C TCATCATIGG G AGTAGTAACC | mboll[dam-] sau3xl mbol[dam-] dpnl ·sfaNI GATCTTC AGCATCTTT | mboli eari rc atactettec |
| r Jam-) TG TCAGAAGTAA NAC AGICITCATI | hphl rsal bsrl scal GACTGG TGAGTACTCA CTGACC ACTCATGAGT | msel hgial dral hgial ahalil bsp12 CT TTAAAAGTGC GA AATTTTCACG | ACT TGA | NTG TTGAATACTC |
| saulAI mbol[dam— dpnI pvuI 4241 CCGATCGTTG 9 | hpt bsrI 1341 CTGTGACTGG GACACTGACC | 4441 TAGCAGAA ATCGTCTT | hgiai bsp1286 apali 4541 CGTGCACCCA GCACGTGGGT | 4641 CACGGAAATG GTGCCTTTAC |
| | | | | |

FIG.-101

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2887

2718

2516 2621

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TAAAAATAGG
ATTTTTATCC
                                                                 bspHI mseI
ATTATCATGA CATTAACCTA
TAATAGTACT GTAATTGGAT
                                                                                                                                                                                                                                                                                                                           17.1 (3. tagI-] 761 2753
1701 2108 2568
767 4411 4793
767 [M. hhaI-] 4411[M. hpaII-] 4.793
3739 3758 4450
72 203 271 522 678 692 1019 1032 1040 2036 2093 2166 2423 2623 2642 2923 3149
3239 3285 3542 4063 4163 4226
318 17 1704 2105 2106 2571 2572 3549 3623 3635 3720 3733 4197 4500 4518
318 317 1704 2105 2106 2571 2572 3549 3623 3635 3720 3733 4197 4500 4518
318 3193 3296 4542
3198 3296 4542
3198 3296 4542
3198 3296 4542
                                                   nlaIII
                                  ahaii
acyi ddei
aatii
C CTGACGTCTA AGAAACCATT A'
G GACTGCAGAT TCTTTGGTAA TI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 1481[dcm-]
816 2105[M.mspI-] 2571[M.mspI-]
767 1086 1129 1326 2374 3823
504[M.haeIII-] 677[M.aluI-] 719 2408
204 207 697 849 940 1017 1033 1236 1443 1467 1596 1599 1722
2905 3324 3389 3392 3598 3926 4115 4292
                                                                                     AAAGTGCCAC
TTTCACGGTG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            716[M.taqI-] 1462
802 1476[dcm-] 1518 1797 4013 4235
453
hinPI
hhaI
thaI
fnuDII
nlaIV bstU[[M.hhaI-]
CAAATAGGGG TICCGCGCAC ATTTCCCCGA
                                                                                                                                                                                                         mnli mboli
4841 CGTATCACGA GGCCCTTTCG TCTTCAA
GCATAGTGCT CCGGGAAAGC AGAAGTT
                                                                                                                                   sau96I[M.haeIII-]
haeIII
                                                                                                                                                                                          eco01091
                                                                                                                                                                             asuI
                                                                                       GARARATARA
CTITITATIT
                                                                                                                                                                                                                                                                                                                                                                                                                                                       alwI(GGATC):
alwNI(CAGNNNCTG):
apaI(GGGCCC):
apaLI(GTGCAC):
aseI(ATTAAT):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       aval(CYCGRG):
avall(GGWCC):
avall(ATGCAT):
ball(TGGCCA):
                                                                                                                                                                                                                                                                                                                                 accI(GT::KAC):
accIII(ICCGGA):
acyI(GRCGYC):
ahaII(GRCGYC):
ahaIII(TITAAA):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             asuI(GGNCC):
asuII(TTCGAA)
                                                                                                                                                                                                                                                                                :Length: 4867
                                                                                                                                                                                                                                                                                                                                                                                                                        alul (EGCT):
                                                                                        4741
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bclI[dam-](TGATCA)

bbvI(GCAGC):

banI

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2540[M.hhaI-]
3939
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          1195
204 207 697 849 940 1002 1017 1033 1236 1245 1324 14443 1446 1453 1467 1596 1599
1722 1803 2516 2538 2552 2621 2718 2771 2887 2905 2908 3026 3181 3324 3389 3392
3598 3926 4115 4265 4292 4387 4616
211 647 855 1271 1281 1426 1452 1574 1671 2043 2144 2520 2540 2564 2582 2584
2687 3028 3609 3939 4432 4764
2687 3028 3609 3939 4432 4764
2887 1393 1122 1143 1718 1807 1885 2046 2657 3855 4036 4323
987 1393 1491 4095
555 1481 2995 3006 3458
153 767 1242 1681 1764 2484 2492 2856 3226
291 505 556 1183 1298 1482 1986 2186 2328 2996 3007 3025 3459 3917 3997 4264
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  3838 4179 4197
                                                                                                                                                                                                                                                                 2520[M.hhaI-]
3609[M.hhaI-]
                                                                                                                                                                               4039 4082
                                                                                                                                                                             3921
                                                                                                                                                                                                                                                                                                                                                                                                                                                   57 473 619 734 1618 1780 2792 3257 3666 3832 4372 4798
139 817 868 1498 1705 2106 2572 3549 3624 3635 3643 3721 3733
4243 4501 4518 4554
3739 3758 4450
2332
290 1481 4263
                                        182 455 1390
295 977 2631 3942 4707
504[M.haeIII-] 677[M.aluI-] 719 1502 2408 2798 3296 4457 4542
3702 4710 4815
                                                                                                                                                                                                                  541 757 1140 1479 3009 3130 3143
211[K.hhaI-] 647 855 1271 1281 1426 1452 1574 1671 2043 2144
2564[M.hhaI-] 2582[K.hhaI-] 2584[M.hhaI-] 2687[M.hhaI-] 3028
4432[M.hhaI-] 4764[M.hhaI-]
                                                                                                                                                                           3398 3515
                                                                                                                                                                          3385
                                                                                                                                                                                                                                                                                                                                          816 867 1704 2105 2571 3623 3634 3720 3732 4500 733 1180 1295 1521 1849 2627 2662 3361 4057 4408 290 1481 4263 57 4780 2792 3257 3666 3832 437 473 619 734 1618 1780 2792 3257 3666 3832 437
                                                                                                                                                                        2250 2729 2757
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           541 757 1140 1479 3009 3130 3143
                                                                                                                                            1701 2108 2568
706 860 1220 1547 1818 1842
4521
778
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             793
801 1475[dcm-] 1517 4850
 3989[M.haeIII-]
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     551 2860 4664
733
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 290
                                                                                                                                                                                                                                                                                                                    Prini(CCANNNNNTGG):
bril(RGATCY):
hril(CCTNAGG):
cril(YGGCG):
cril(YGGCCR):
cli(ATCGAT):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 ecoll(CTCTTC):
ecoll(CCTNAGG):
ecoll(CCTNNNNAGG):
by LI (GCCNNNNNGGC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 draI(ITTAAA):
draIII(CACNNNGTG):
eaeI(YGGCCR);
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 "COOLOGI (RGGNCCY):
                bylli(AGATCT):
bral(GAATCT):
bral(GAATCC):
bral(GTCTC):
bral(GTCTC):
brapHI(TCATCA):
brapHI(ACCTCC):
brapHI(ACCTCC):
brapHI(ACCTCC):
brapHI(ACCTCC):
                                                                                                                                                                                                              bath (TICGAA):
bath (CCMG):
bath (GGCG):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         eroRI (GAATTC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               ecoRV(GATATC):
Inu4HI(GCGGC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             ecoRII(CCWGG):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                fspl(TGCGCA):
hael(WGGCCA):
haell(RGCGCY):
haell(GGCC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  fmuDII(CGCG):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             tokI(GGATG)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                          ding I (GATC):
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-1G.—10K

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71 691
623[M.taqI-] 628[M.taqI-] 776[M.taqI-] 1341[M.hphI-] 1562[M.hphI-] 2068 2264
2286 2882 2957 3353 3870
1171 1180 1295 1321 1522 1702 1849 2109 2439 2569 2628 2662 3189 3336 3362 3552
3956 3990 4057 4167 4409
380 1136 1344 1565 2346 2592 2601 3726 3953 4349 4575 4590
409 514 551 744 842 870[dam-] 1638 2465 2861 3632[dam-] 3723[dam-] 4478 4556[dam-]
4665 4861
139 817 868 1498 1705 2106 2572 3549 3624 3635 3643 3721 3733 3838 4179 4197
                                                                                                                                                                                                                                                                                                                                                                                                      4243 4501 4518 4554
148 163 241 372 378 554 606 610 639 650 682 736 771 809 835 1013 1125 1185 1265
1303 1330 1516 1830 1888 1944 2372 2579 2609 2871 3097 3154 3421 3821 3902 4032
4238 4849
62 257 324 1044 1066 1757 1979 2011 2125 2136 2148 2159 2176 2274 2545 2763
368 83 3740 3745 3759 3812 4047 4086 4451 4823
1171 1180 1295 1321 1522 1702 1849 2109 [M.bamHI-] 2439 2569 [M.bamHI-] 2628 2662
3189 3336 3362 3552 3956 3990 4057 4167 4409
1320 2438
160 1295 1521 1849 2627 2662 3361 4057 4408
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     123[M.alur-] 1239
10 964 1288 1495 1629 1854 1918 1983 2618 2723 2983 3703 4194 4204 4282 4318
1711 4816
104 767 816 1086 1129 1291 1326 1361 1475 1518 1797 2105 2374 2395 2407 2571
1012 3051 3823 3917 3958 4169 4759
                                                                                    2541
4765
2541
4765
                                                                                      2519
4433
2519
4433
                                                                                    2493
4096
2493
4096
                                                                                   2485
4003
2485
4003
                                                                                    1765
3610
1765
3610
917 1277 1427 2041 2565 2688 3084 3662 4412 677 [M.alur-] 1502 2798 3296 4457 4542 767 1086 1129 1326 2374 3823 504 677 719 2408 1111 1243 1394 1456 1492 112 154 210 768 988 1111 1243 1394 1456 1492 112 154 210 768 988 1111 1243 1394 1456 1492 1112 154 210 768 988 1111 1243 1394 1456 1492 12563 2583 2686 2716 2857 2890 3160 3227 3327 3477 [M.taqr-] 4414
                                                                                   1492
3327
1492
3327
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   716
14 1352 1401
2264 2286 2882 3353 3870
801 1475 1517
590 4116[M.H1-]
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 53
853 2617 2982
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   nspCix(RCATGY):
paeR7I(CTCGAG):
ptlMI(CCANNNNTGG):
                                                                                                                                                                                                                                                                                                                                                                                          mior(dam-)(GATC):
                                                                                                                                                                                                                       h:ndIII(AAGCII):
h:nfI(GANIC):
                      hqiai(GWGCWC):
hgici(GGYRCC):
hqiji(GRGCYC):
hhai(GCGC):
                                                                                                                                                                  hinc[I(GTYRAC):
hindII(GTYRAC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               mstI(TGCGCA):
mstII(CCTNAGG):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 pleI(GAGTC):
ppuMI(RGGWCCY):
pstI(CTGCAG):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           ncil(CCSGG):
ndeI(CATATG):
nheI(GCTAGC):
nlaII(CATG):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    nael(GCCGGC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       IN FI (GGCGCC):
                                                                                                                                                                                                                                                                                                                              hphI(GGTGA):
mboII(GAAGA):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     nlaIV(GGNNCC)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            nruI(TCGCGA):
nsiI(ATGCAT):
                                                                                                                           hinPI(GCGC):
                                                                                                                                                                                                                                                                                     (5555) II (-65)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      : (5555)Idem
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             msel(TTAR):
                                                                                                                                                                                                                                                                                                                                                                                                                                   mnlI(CCIC)
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AFILI(CTTEAG), asp718(GGTACC), avrII(CCTAGG), bssHII(GCGCGC), bstEII(GGTNACC), espI(GCTNAGC), hpaI(GTTAAC), kpnI(GGTACC), mluI(ACGCGT), ncoI(CCATGG), notI(GCGCCGC), rsrII(CGGWCCG), sfiI(GGCCNNNNNGGCC), smaI(CCCGGG), sphI(GCATGC), xmaI(CCCGGG)
3082 4526
2144 2520 2540 2564 2582 2584
                                                                                                                                                                                                                                                                                                                                           867 1704 2105 2571 3623 3634 3720 3732 4500 4517
                                                                                                                                                                                                                                              555
567 1406
478 486 626[M.claI-] 717 779 894 975 1305 2370
211 647 855 1271 1281 1426 1452 1574 1671 2043
2687 3028 3609 3939 4432 4764
968 2726
                                                                                                                                                                                                                                                                                                                                                                   2068 4470
                                                                                                                                                                                                                                                                                                                                716
816
290
623
                                                                                                                                 scal(AGTACT):
scrFI(CCSGG):
scrFI(dcm-1(CCWGG):
staNI(GCAIC):
                                                                                                                                                                                                                                                                                                         tth1111(GECNETIGEC):
                                                                                                                                                                                                                                                                                                                   rsal(GTAC):
saci(GAGCTC):
sacil(CGGCGG):
sall(GTCGAC):
                                                                                                                                                                                                                                              #thI[AGCCT]:
styl(CCWAGG):
taql(ICGA):
   pruI(CGATCG):
pruII(CAGCTG):
                                                                                                                                                                                                       spel(ACTAGT):
zspl(AATATT):
satl(GAGCTC):
                                                                                                                                                                                             snaBI(TACGIA):
                                                                                               sau96I(GGMCC)
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₩01-191

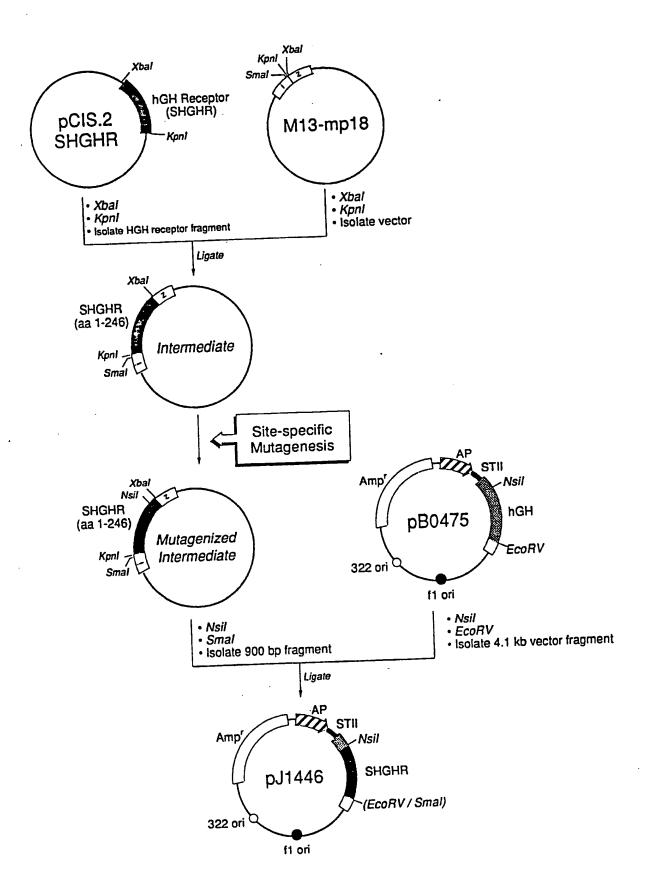


FIG.-II
SUBSTITUTE SHEET

| ပ္ပပ္ | HG FIG | HÜĞ | | н | |
|--|---|---|----------------------------------|---|---|
| ACTGCAATGC TGACGTTACG | ACGACGATAC TGCTGCTATG | haelli laili laili lei bsmal GGCCGAGACT | AAA TTT LYS | haell hael nnll sag gcc trc cgg | CCT GGA Pro |
| ACTG | ACGA | haell xmalll eagi eael cfrl b C GGCCG | ATG TAC Met | a Eggg | nlaIV G GAG C CTC 'S Glu |
| GTC | CTG | | HÆ | AGT TCA Ser | HA HA |
| GATTATCGTC | bsmI AGCATTCCTG TCGTAAGGAC | xmetales | ohi E GTGATTTT CACTAAAA | GGA | ddei III TCT A AGA T |
| | | | | TCT | mboli TCT T AGA A |
| II PIGGA | sfani GATGCC CTACGG | CATA | mnl Trgag | TTT AAA | A AAT TTA |
| aluI hindIII I AAGCTTTGGA TTCGAAACCT | sfaNI GCCCGATGCC CGGGCTACGG | aluI uII AGCTGTCATA TCGACAGTAT | hi AGAGGTTGAG TCTCCAACTC | nsil avalli AT GCA ATA CGT | A ACA |
| a) | | • | | HAH | -] AAG TTC |
| ms. GTTGTTATTT CAACAATAAA | I mnli ACGAGGTAAA TGCTCCATTT | p TCTTTTCAAC AGAAAAGTTG | xba. AAGGGTATCT TTCCCATAGA | r GCC A CGG | haeIII stul[dcm-] haeI scrFI[dcm-] ecoRII bstNI CCA GGC CTA GGT CCG GAT Pro Gly Leu |
| GTIG | I mnli ACGAGG TGCTCC | TCTT | AAGG TTCC | A AAT I ITA I Asn | hae: stul[c hae] scrF1[dc ecoR1] bstN1 CCA GGC GGT CCG |
| | | | | T ACA A IGI a Ihr | H G C B B B |
| dde.i TCATTGCTGA AGTAACGACT | hinPI hhaI . haeII rs: GGGCGCTGT | mseI AAAAAGTTAA TTTTTCAATT | TTCACGTAAA AAGTGCATTT | T GCT A CGA e Ala | mseI GTT AAT CAA TTA |
| TCA | | | | TCT ATT AGA TAA Ser Ile | |
| aIII ATGAAAAATC TACTTTTTAG | laar [dam-] [dam-] mnlr rcaggragag Agrccarcrc | mnlI CCTCGTCAGT GGAGCAGTCA | rsaI AGTACGCAAG TCATGCGTTC | TIT TCT AAA AGA Phe Ser | CAA AGT GTT TCA |
| nlaiii C ATGAA G TACTT | sau3AI mbol[dam-] dpnI cll[dam-] GA TCAGGIZ | mnl1 CCTCG | rsaI GTAC | GTT T | CTG GAC GAC GAC GAC |
| | | нн | ₩ | TTC G AAG C Phe v | _ |
| n] AAATACAGAC TTTATGTCTG | sav mbo dpi bcll GGTTGATTGA CCAACTAACT | fok sfan ATTGAAGCAT TAACTTCGTA | spe. Attigtaact Taaacattga | ATG T TAC A | ⊣⊹⊣ত |
| AAA | GGT | ATTC | ATT TAAZ | CT GA | רונים ח. |
| AAGG | CAGC | AGTT | I ATGT TACA | sfani GCA T CGT A | hgiai bsp1286 AGA GCA (FCT CGT (Arg Ala B |
| TTGGATAAGG AACCTATTCC | GACCAACAGC | .i-) Taaagaagii Atticaa | mseI TTTTTAATGT AAAAATTACA | CTT GAA Leu | hgi bsp AGA TCT Arg |
| | | M.hhaI- snaBI TACG T? | | mboII TTT CTT AAA GAA Phe Leu | ddel CTT AGC GAA TCG Leu Ser |
| PflMI TCTCCATACT AGAGGTATGA | hinPI hhai GGCGCAAAAT CCGCGTTTTA | thaI I fnuDII bstUI[M.hh nPI snaB aI snaB CGCGATTACG | TTGTTTTAT AACAAAAATA | | |
| TCTC | hinP] hhai GGCGC2 CCGCG | thai fnu4HI bbvi fnuDII 4HI bstUI[M.hhai-] I hinPI snaBI hhai snaBI GCTG CGCGATTACG TAA | TIGI | GCA CGT Ala | ATC |
| ACT | TAT | | GCT | ATC TAG | aluI fnu4HI bbvI GCA GCT CGT CGA |
| ecoRI GAATTCAACT CTTAAGITGA | TTCGCAATAT AAGCGTTATA | fnu41 bbvI fnu4HI bbvI h; aluI h} GGAGCIGCTG | TATAGICGCI ATATCAGCGA | AAT TTA | h GC GC Al |
| ecoRI 1 GAATT CTTAA | | | | 5 AAG TTC 1 Lys | 6 ACA IGI 7 Ihr |
| | 101 | 201 | 301 | 395 | 476 |
| | | | | | |

F1G.—12A

| styl avrii AG AAC TC TTG | | | | Li | |
|--|---|---|--|---|--|
| st AAAC ATTG ASD | GTT CAA Val | AAT TTA Asn | TTA AAT Leu | foki GGA CCT Gly | ACA TGT Thr |
| AAG TTC Lys | TAT ATA TYF | AGC TCG Ser | ACT TGA | AAA TTT Lys | acA TGT |
| ACA TGT | GAT CTA ASP | ACT TGA Thr | i TGG ACC TFP | CAG GTC Gln | TTG AAC Leu |
| | CCT GGA Pro | CTA CTA GAT Leu | bsrI AAC TGG TTG ACC ASn Trp | ATT TAA Ile | ATA TAT Ile |
| rse nlaili CAT GGT GTA CCA His Gly | TGC ACG Cys | aluI AAG CTA TTC GAT LYS Leu | li CTC GAG Leu | GAT CTA ASP | CCT GGA Pro |
| CAT GTA His | bsmI GAA Glu | ATC TAG Ile | mn GCC CGG | GCA CGT Ala | saugei nlaiv avaii asui nc cac |
| COTT CAAA Val | AAA TTT Lys | TGT ACA Cys | ATT TAA Ile | AAT TTA ASD | sa av as ATG TAC Met |
| mnli GAG (CTC (| TGG | TAT ATA TYE | CCC GGG Pro | CGC GCG Arg | ATG TAC Met |
| GAT CCTA CASP | GAA CTT Glu | CCT GGA Pro | sau3AI mboI[dam-] dpnI alwI xhoII bstYI AA CCA GAT CCA CCC TT GGT CTA GGT GGG | CCA GGT Pro | AAA TIT Lys |
| ACA C TGT C | CAA GTT Gln | ATA TAT Ile | sau3 mboi dpni alwi toli ftyi GAT CTA | GCA CGT Ala | TGG ACC Trp |
| ir CGG Tr | pleI hinfI G ACT C TGA | TGG ACC Trp | xh CCCA GGT | GAA CTT Glu | AAA TTT Lys |
| bsr] CAC 1 GTG 7 His 1 | Pl pl rgg ACC rrp | 무원은 | CAA GIT Gln | IGG ACC Trp | ACT TGA Thr |
| ricc o | GAA CTT Glu | mnll ACC TCC A TGG AGG T Thr Ser I | GTG | AGA TCT Arg | GAA CTT Glu |
| nlaIII TCA TGC AGT ACG Ser Cys | CAA GII | mnli ACC TC TGG AC Thr Se | ATA TAT Ile | GTG CAC Val | AAT TTA ASD |
| TTT AAA Phe | ACT TGA Thr | TTT AAA Phe 26: | GAA | CAA GTT GIn | GTA CAT Val |
| HAH | AAC TTG Asn | TCG 3 AGC 1 Ser 1 from | GAT CTA ASP | ecoRV GAT ATC CTA TAG ASP Ile | GAA CTT Glu |
| bsmal GAG A(CTC T(Glu T) | AGG TCC Arg | AT TCA TA AGT Sn Ser differ | GTT CAA Val | | AAA TTT Lys |
| CGA GCT Arg | AGA TCT Arg | HAHA | TCT AGA Ser | LII GCA CGT Ala | TAC |
| ir GAG CTC Glu | ACC TGG Thr | E ~ # % | TTC AAG Phe | nlaiii CAT GC2 GTA CG3 His Ala | CAA GTT Gln |
| dde CCT GGA Pro | TAT ATA TYr | TAC ATG TYF t 9 k | TGT ACA CYS | Infi ATT TAA Ile | CTT GAA Leu |
| hphi TCh AGT Ser | TTC AAG Phe | TCT ACA CYS | AAG TTC Lys | I bj GGG CCC Gly | GAA CTT Glu |
| CGT GCA Arg | LI CTG GAC Leu | alui vuii AGC TCG Ser | GAA CTT Glu | osr ACT FGA Fhr | TAT ATA TYT |
| TGC ACG Cys | aluI pvuII CAG CTG GTC GAC | alul pvull AAC AGC TTG TCG Asn Ser these f | foki G GAT G C CTA C | msel TTA A | G&G CTC Glu |
| AAG TTC Lys | ATA TAT Ile | GAA CII Glu | for CAC | AGT TCA Ser | CTG GAC Leu |
| III CC GG hr | I I I I I I I I I I I I I I I I I I I | 988 666 617 | i ACA TGT Thr | GTC CAG Val | GTT CAA Val |
| dra hphi TTC A AAG T | sau961 nlaIv avaII asuI ppuMI ecc01091 | GCT CGA Ala | rsa GGT CCCA G1Y | AAC TTG | Coki SG ATG CC TAC |
| rrr TTT Lys | PP CT & CGAT CAT | TCT AGA Ser | GGT | CTG | fok TGG ACC |
| 34 | 638 | 713 | 800 | 142 | 962 |
| | | | | | |

F16.-12E

| TAT ATA TYr | H HH HH | STIG | II CCCT GGGA |
|--|---|---|---|
| STATE TO THE TOTAL | haeIII xmaIII eagI eaeI cfrI notI fnu4HI iG CG | bsmI TTTCACTGC ATTCTAGTTG | fnu4HI hinPI hhaI eII GCGCCGCCT |
| 668 617 617 | ha xma eag eag eag notI fnu4HI TAG CG | bsmI GC AT | ď |
| TCT AGA Ser G | TAC TI | GACC | f nheI hin fnu4HI hhaeII bbvI haeII GCTGCTA GCG |
| AAC TC TTG AC | TTC TA | TTCA | nheI fnu4HI bbvI he CGTGCTGCTA GCACGACGAT |
| CGA AL | | | |
| CAA CCGIT GCIN A1 | OII T CAT U ASP | CALT | TATG |
| - 450 | mboli GAA GAA GA CTT CTT CT | TAAAGCATIT ATITCGIAAA | [GTCACTATGG CAGTGATACC |
| lda SSC fa | | | SrI Gradi |
| sau3AI mbol[dam— dpnI alwI xhoII bstYI AGA TC AAI TCT AGG TT' Arg Ser LY | nlaIII nspCIX ACA IGT TGT ACA Thr Cys | ATTTCACAAA TAAAGTGTET | sfaNI bsrI GCATGGCCA CGTAGCGGT |
| SGTG ACCORD | nla nsp(TTT ACA AAA TGT Phe Thr | ATTT | sfaNI bsrI AGCATCGCCA TCGTAGCGGT |
| CGT G GCA C. | CAA T7 GTT A1 | CAA | |
| GTG C CAC G Val A | | sfaNI AGCATCACAA TCGTAGTGTT | CCATTCCGAC GGTAAGGCTG |
| GAA G CIT C | ATG AGC TAC TCG Met Ser | | |
| TAT G ATA C TYr G | al CCAG ATG GTC TAC | CAA1 | I-] |
| GAA I CIT A | ddei mnli CCT C2 GGA G7 | ATAAAGCAAT TATTTCGTTA | sau3AI mbol[dam-] dpni alwi hoII luV stYI anHI lwI C ATCCCATCGT |
| AAG G TTC C Lys G | CTT CCTA CGAA GC | | |
| GAT A CTA 1 | ACA CI TGT G7 | TGGTTACAA | хаддабо |
| GTG CAC CAC CAL | GTA AC CAT TC | ATGGTTACAA PACCAATGTT | nlaIII CATGTC |
| AAA G TTT C Lys V | TAT G TYT C | ~ = | HA |
| TTG P AAC T Leu I | 10 C1C2 T | alui fnu4Hi bbvi GCAGCTTATA | ATGTATCTTA |
| TCA 1 | hgiai bsp128(I GTG CTC CAC GAC | aluI fnu4HI bbvI GCAGCT | ATGI |
| TALLE TALLE | h b b corc corc corc corc | IATT | ATCA |
| GT CAC Val | AGT GE | CTTGTTTATT | AAACTCATCA |
| beri CC: G GGI C Pro v | TTC ACPAGE | HH | |
| GTT CAN PGCAN PROBLEM | GAG IC | msel hpal hindil hincil I I I I I I I I I I I I I I I I I I I | GTCC |
| TCA Set V. | 000 000 017 017 | msei hpai hindi hinci thai fuuDii bstUi fuuHHI GCCGCGTTAA | TGGTTTGTCC |
| e 9 | 124 GC 223 G | 01 GC | |
| 104 | 11 | 120 | 1301 |

FIG.—12C

| | | 0 1/2 | |
|--|---|---|---|
| hphi pflMi hinfi[M.hphi-] CGCTARCGGA TTCACCACTC | AACICCICAC thaI fnu4HI fnuDII bbvI bstUI GCAGCGGAC | bsri CCTTACTGGT GGAATGACCA | GGTTTCCGTG |
| | | GGCGGGGTTG | nlaIII mboII CAACAACATG AATGGTCTTC GTTGTTGC TTACCAGAAG |
| mnli nlalv mspi hgiCi hpair bani nael fnu4HI AATGGAAGCC GGCGGCACT | hgaI thaI fnuDII bstUI AGAACATATC CATCGCGTCC TCTTGTATAG GTAGCGCAGG | mspI hpaII scrFI scarFI sau96I nlaIV avaII avaII ppuMI eco0109I mnlI cauII GTTGAGGACC CGGCTAGGCT | ddei GCGACCTGAG CAACAACATG A CGCTGGACTC GTTGTTGTAC T |
| I . [M.haeIII-] taqI mnli CCTCGACCTG GGAGCTGGAC | LMI Styl AACCCTTGGC TTGGGAACCG | CTGTC | fnu4HI bbvi 4HI GCTG CAAAACGTCT GCG? CGAC GTTTTGCAGA CGC? |
| sc nc ns nlall nlall ca rgcargg AGCC | hinPI msti fspi bsmI hhal pflMI styI TTCTTGCGGA GAACTGTAA TGCGCAAACC AACCCTTGGC | hi hi hi hi hi hi hi hi hi hi hi hi hi h | fnu4HI bbvI fnu4HI bbvI ACGIGAAGCG ACTGCTG CAAAACGTCT TGCACTTCGC TGACGACGA |
| tha! fnuDII fnuDII bstUI hga! CG CGTTGCGTCG CGG | | hae scrFl ecoRl bstNl sau961[d avall[dc aval eae ppuMl cfr nlaly bal ecoOl091[| thal fnubli bstUl -) ACGCGAGCGA TGCGCTCGCT |
| th fr mnll bs c recereces | | sfaNI hinPI fnu4HI fnu4HI avaI bbvI GCGCGCATC TCGGCAGCG | hphi hinfi[M.hphi TAGCAGAATG AATCACCGAT ATCGTCTTAC TTAGTGGCTA |
| 1 ATACCTIGIC TAIGGAACAG | | | hphI hinfI[M.hphI 1701 TAGCAGAATG AATCACCGAT ATCGTCTTAC TTAGTGGCTA |
| 1401 | 1501 | 1601 | 170 |

FIG.—12D

| | ្តប | HHHHH CO | ∢ ₽ | ÆH | ⊄ F4 |
|--|--|---|--|--|--|
| | CACCTACATC GTGGATGTAG | scrFI nc11 mspI hpaII cauII | sfaNI mnli GGAGGCATCA CCTCCGTAGT | thai fnuDii bstui i foki CGCGGATGAA GCGCCTACTT | msel thar fnuDII bstVI TCGCGTTAAA |
| | | bsrI C CAGI G GTCA | | thaI fnuDII bstVI aI fok CGCGGA | |
| | IGGAA | b CGTTC SCAAG | FACAC | II hg | msel TTAAAT |
| | CCCTGTGGAA | scrincii ncli nspi hpal bsri caul CACAACGTC CAGTAACCGG | CCCCITACAC GGGGAATGTG | th ful bs aluI hgaI ACGAGCTGGA CG TGCTCGACCT GC | msel TTGTTAAAAT |
| | GCTA | | | CTCA | PI TATT |
| | fnu4HI bbvI iNI :G CTGCTGGCTA | mnl) TGTTTACCCT ACAAATGGGA | ACAGAAATTC TGTCTTTAAG | GAGAAACTCA CTCTTTGAGT | sspi msei CGTTAATATT GCAATTATAA |
| | EDH | | | | HI-] STAAA CATTT |
| _ | f CGCAG | bsrI TACCGCCAGT ATGGCGGTCA | nlaiii ACCCCCATGA TGGGGGTACT | ACGCT TGCGA | mspI[M.bamHI-] hpaII spMII ccIII 3AI I[dam-] I[dam-] I I CGG AAATTGTAAA GGCC TTTAACATTT |
| sau3AI mbol[dam-] dpnI holl stYl | sfani GCA I | | | mseI ATT A TAA T | |
| sau3AI mbor[d dpnI xhoII bstYI | PIT E STANI STANI CGGATCTAC ACCTACATOL ACCTACATOL CCCTACATOL ACCCTACATOL ACCTACATOL ACCTACATOL ACCCTACATOL ACCTACATOL ACCTACATOL ACCCTACATOL ACCTACATOL ACCTACATOL ACCTACATOL ACCATOCATOL ACCATOCATOCATOL ACCATOCATOCATOCATOL ACCATOCATOCATOCATOCATOCATOCATOCATOCATOCA | foki sfani fnu4HI GCCGCATCCA | CGGTATCATT GCCATAGTAA | msel GCCAGACATT AACGCTTCTG CGGTCTGTAA TTGCGAAGAC | mspI hpall bspMIl sau3AI mboI [dan dpnI alwI nlaIV bstYI bamHI [M.n alwI CAGGATCCGG |
| | mspi hpali bspMil accili ITC CGG | | | ≪ ∺ | |
| | me hp bsp acc CATTATGITC GTAATACAAG | sau96I nlaIV avaII asuI CTCTGGTCC | CTCGTTTCAT GAGCAAAGTA | sau961[M.haeIII-] haeIII asuI III CGCCCGC TTTATCAGAA | aluI AGCTTTACCG TCGAAATGGC |
| | | | | Σ | |
| | nPI ai II CGCCCTGCAC GCGGGACGTG | AGTGATTTT TCACTAAAAA | mnli foki sfani agcarctrr | sau961[l haelli asul nlalli CATGGCCGC | CACGCTGATG |
| | ·H C (1) | □ | | nla CAT GTA | |
| | h AGTCA | dder ATTGACCCTG TAACTGGGAC | CCGTATCGTG | mse] CTTA? | GCTTCACGAC |
| | thal fnuDII bstUI kCG CGGA | | CCGT | mseI CCGCCCTTAA GGCGGGAATT | GCTTC |
| | thal fnuDi bstU hhhCG CG | ri I CTGGC | STAAC | | xmnI hinfI GAATC CTTAG |
| | thal fubli his pictory process contracts between the particle contracts between the process of t | hinPI hhaI haeII AAGGGTGGC | CATCAGTAAC GTAGTCATTG | CAGGAAAAAA GTCCTTTTTT | xmnI hin£I TCTGTGAATC AGACACTTAG |
| | AAAG TTTC | | I TCAT AGTA | | |
| | TTTCGTAAAG AAAGCATTTC | msel TGTATTAACG ACATAATTGC | nlalii nspcix GCATGTTCAT CGTACAAGTA | AGTGACCAAA TCACTGGTTT | CAGGCAGACA |
| | 1861 7 | 1901 T | 2001 | 2101 Å | 2201 C |
| | | | | | |

F16.-12E

| | - | 1012 | TAICCGGCTT | TURCCRITTE | AGGGAATATT | TAGTTTTCTT | ATCTG | | ACAACAAGGT |
|-------|---|---|---|--|---|--|--|--|---|
| - X E | hinfi Agagrccact TCTCAGGTGA | msel ATTAAAGAAC TAATTTCTTG | Plei hinfi GTGGACTCCA CACCTGAGGT | ACGTCAAAGG TGCAGTTTCC | GCGAAAAACC CGCTTTTTGG | GTCTATCAGG CAGATAGTCC | haeIII asuI GCTATGGCCC CGATACCGGG | ACTACGTGAA TGATGCACTT | hphi CCATCACCCT GGTAGTGGGA |
| Hat | mi taq] TTGGGGTCG AACCCCAGC | nlaIV hgiCI mnlI taqI banI TTTGGGGTCG AGGTGCCGTA | AAGCACTAAA TTCGTGATTT | nlaIV TCGGAACCCT AGCCTTGGGA | hgiJII bsp1286 banII nlaIV AAAGGAGCC CC | 6 CCCGATTTAG GGGCTAAATC | alui AGCTTGACGG TCGAACTGCC | mspi hpali nael GGAAAGCCGG C | CGAACGIGGC |
| 90 | mboli GGGARGAAAG CCCTTCTTTC | CGAAAGGAGC C | hinpi hinpi hhai hhai haeii haeii GGGCGCTAGG GCGCTGGCAA | | GTGTAGCGGT (| thai fnubli bstull hinri hhai fnu4Hi bbvi CACGCTGCGC GT | thai fnubii inPi hai CGC GTAACCACCA | hinpi hhai thai thai fundii hin bstufM.hhai-) fnu4Hi msei hha CACCGCCGC GCTTAATGCG GTGGGCGCG CGATTACGC | hinpi hhai fnu4Hi thai fnu01I hinpi bstUI[M.hhai-] U4HI mseI hhai CGC GCTTAATGCG |
| EE00 | sau3AI mbol[dam-dpnI alwI alwI xholI nlalV bstxII bstMII bstWII[M.ms; thal mspl[M.bamHI] fnubII alwI bstUl[M.hhal-] hinPI hpaiI hhal accili ngGCGTCGG ATCCTGC | u3AI n1 MI WI IV YI IV M. bamHI-] I fh aI-] bs ATCCTGCCTC | thaI fnuDII hinPI thaI fnuDII bstUI[M.hhaI-] c GCGCGTTTCG GTGAT G CGCGCAAAGC CACTA | hai nubii stui[M.hhai-] npi npi 1[M.hhai-] i[M.hhai-] GCGTTTCG GTGATGACGG TGAAAACCTC GCGCAAAGC CACTACTGGGG | | fnu4HI bbvI nlaiII nspCIX alu TGACATGC AGC | bsn mspi hpali 4HI scrfi I ncii cauli alui | aI al | LuI |

FIG.—12F

hinPI haII haeII aluI CTTCGGGAAG CGTGGCGCTT TCTCATAGCT CACGCTGTAG

GCCTTTCTCC CGGAAAGAGG

hinPI mnll hhaI CCCTCGTGCG CTCTCCTGTT CCGACCCTGC CGCTTACCGG ATACCTGTCC

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| bsri nlaili CATGACCCAG TCACGTAGCG ATAGCGGAGT GTACTGGGTC AGTGCATCGC TATCGCCTCA | sfani CGCACAGATG CGTAAGGAGA AAATACCGCA GCGTGTCTAC GCATTCCTCT TTTATGGCGT | A AAGGCGGTAA TACGGTTATC I TTCCGCCATT ATGCCAATAG | II I I TGCTGGCGTT TTTCCATAGG | scrFI[dcm-] scrFI[dcm-] ecoRII bstNI bstNI AAAGATACCA GGCGTTTCCC CCTGGAAGCT TTTCTATGGT CCGCAAAGGG GGACCTTCGA |
|---|--|--|--|--|
| H | | : alui AGCTCACTCA TCGAGTGAGT | thai fnubli bstUl fnu4HI haeIlI AAGGCGCGT | scrFI ecoRI bstNI AAAGATACCA G TTTCTATGGT C |
| fnu4HI bbvI hinPI hhaI GGGGCGCAGC | TGTGAAATAC ACACTTTATG | fnu4HI fnu4HI bbvI CGGCTGCGGC GAGCGGTATC | scrfi[dcm-] ecoRii bstNi eIII I nlaIV CCAG GAACCGTAAA | ACAGGACTAT TGTCCTGATA |
| GGCGGGTGTC | s6 ndeI CCATATGCGG GGTATACGCC | fnu4HI fnu4HI bbvi cccTGCGGC GCCGACGCCG | scri[dcm-] ecoRII bstNI haeIII haeI nlaIV AAAAGGCCAG GAACCGTAAA | GCGAAACCCG ACAGGACTAT CGCTTTGGGC IGTCCTGATA |
| hgal thai fnuDII bstUI[M.hhaI-] hinPI hhaI AGGGGGGTGT TCCCGCGCAGAA | hgiai ddel bsp1286 rsal apali CAGATIGTAC TGAGAGTGCA CI GTCTAACATG ACTCTCACGT G | PI I CTCGGTCGTT GAGCCAGCAA | haeIII haeI AA.GGCCAGC TTTCCGGTCG | mnlI GTCAGAGGTG CAGTCTCCAC |
| | | hinPI hhai hhai mnli hinfi bbvi TICCGCITCC TCGCTCACTG ACTCGCTGCG C | nlaiii spcix cargrgagca Gracacrcgr | hgaI IqI CGACGCTCAA GCTGCGAGTT |
| CAAGCCCGTC | sfaNI msel fnu4HI TTAACIATGC GGCATCAGAG AATTGLTACG CCGTAGTCTC | LI TCGCTCACTG AGCGAGTGAC | nlaiii nspcix CAGGAAAGAA CATGTGAGCA GTCCTTTCTT GTACACTCGT | ts TCACAAAAT AGTGTTTTA |
| scrFI ncil mspI hpaII sfaNI fokI cauII AGCGGAGC CGGGAGA | msel TTAACTATGC AATTG%TACG | III mnli TICCGCIICC I | GGGGATAACG CCCCTATTGC | sfah CTGACGAGCA GACTGCTCGT |
| scrFI ncil mspi hpali sfaNI foki cauli iAGCGATGC CGGC | bsrI accI GTATACTGGC CATATGACCG | mboli eari hinpi hhai haeli 1841 TCAGGGGTC TT AGTCCGGGG AA | hinfI 1101 CACAGAATCA GTGTCTTAGT | hgaI SfaNI taqI SAGGCGGGG GACTGCTCGT AGTGTTTTA GCTGCGGTT |
| 2901 | 2901 | 3041 | 3101 | 3201 |

| | | [- | | | |
|---|---|---|--|---|---|
| CTATCGTCTT GATAGCAGAA | GAGIICIIGA CICAAGAACI | mspI hpali sau3AI mbol[dam- dpnI aluI alwI A GCTCTTGATC | -] sau3xI mboI[dam-] dpnI GATCTTTCT | .I msel Aattaaaat Ttaattaa | am- GTCTATTCG CAGATAAAGC |
| mspi hpali TATCCGGTAA ATAGGCCATT | CGGTGCTACA | al AGAGTTGGTA TCTCAACCAT | sau3AI mbol[dam-] dpnI alwi xholl bstyl mboll[dam-] G AAGATCCTTT G | sau3AI mbol[dam-] dpnI alwI mseI xholi draI bstYI ahallI A GATCCTTTTA AI T CTAGGAAAAT T | sau3AI mboi[dam-] ddeI dpnI C TCAGCGATCT GTCT2 |
| hinPI hhaI fnu4HI bbvI cGCTGCGCCT GCGACGCGGA | .I GGTATGTAGG CCATACATCC | CTTCGGAAAA GAAGCCTTTT | sau3AI mbol[dammbol[dammbol[dam-] dpnl alwi xhoII xhoII xhoII xhoII bstYI bstYI mboIl[dam-] GGATCTCAAG AAGATCCTTT CCTAGAGAAA | holl[dam-] [dam-] xh hphl bs CTTCACCTA | laiv giCi ani GCACCTAT |
| TCAGCCCGAC | mnli AGCAGAGCGA TCGTCTCGCT C | bsrI AGCCAGTTAC TCGGTCAATG | M.hhaI-) AGAAAAAA TCTTTTTT | m sau31 mbol dpni xhoII bstYI alwI ACTTTTCCT AG | mn] ATCAGTGA TAGTCACT |
| AACCCCCGT TTGGGGGGCA | TAACAGGATT ATTGTCCTAA | hinPI hhai GC GCTCTGCTGA CG CGAGACGACT | r AGATTA TCTAAT | nlaIII bspHI T CATGAGATTA A GTACTCTAAT | |
| hgiai bsp1286 apali rgrgrgcacg acacacgrgc | fnu4HI fnu4HI bbvI alwNI bsrI bbvI bsrI CCACTGGCAG CAGCCACTGG | TGGTATCT | fnu4HI bbvI TGCAAGCAGC ACGTTCGTCG | bs GGATTTTGGT CCTAAAACCA | GTCTGACAGT |
| aluI CAAGCTGGGC GTTCGACCCG | fnu fnu4HI bbvI a bsrI bbv CCACTGGCAG C | GGACAGIAIT CCTGTCAIAA | TTTTTTGTT AAAAAACGA | mseI TCACGTTAAG AGTGCAATTC | AGTAAACTTG TCATTTGAAC |
| TCGTTCGCTC | CGACTTATCG GCTGAATAGC | TACACTAGAA ATGTGATCTT | GTAGCGGTGG | GAACGAAAAC | AGTATATATG TCATATATAC |
| T TCGGTGTAGG A AGCCACATCC msp1 | hpair screi screi noti cauli chifi cauli CTCAACC CGGTAAGACA | II TAACTACGGC ATTGATGCCG | ACCACCGCTG | hgal ddel ACGGGGTCTG ACGCTCAGTG TGCCCCAGAC TGCGAGTCAC | I ATCAATCTAA TAGTTAGATT |
| ddei GTATCTCAG CATAGAGTC | | haeIII haeI AGTGGTGGCC T | CGGCAA.CAA | hç ACGGGGTCTG TGCCCC.GAC | msel drai abalii GAAGTTTTAA |
| 3401 | 3501 | 3601 | 3701 | 3801 | 3901 |

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| | | | | | ı II |
|---|---|---|---|--|---|
| bsmal I DII UI G AGACCCACGC | mseI aseI TCTATTAATT AGATAATTAA | CGTTTGGTAT GCAAACCATA | [sau3AI hbol[dam-] dpnI bvuI CGATCGTTGTC | hphi bsri GTGACTGGTG CACTGACCAC | msel drai J ahaiii GCAGAACTTT CGTCTTGAAA |
| bsmaI thaI fnuDII bstUI TGATACCGG AGACCCACGC | bsrI mnll fokl CTTTATCCGC CTCCATCCAG GAAATAGGGG GAGGTAGGTC | TCACGCTCGT | mnli sau961 avali asul TCGGTCCTCC AGCCAGG | | hinPI hhai thai fnuDII bstUI(M.hhaI-) C GCGCCACATA G |
| sau96I[M.haeIII-] nlaIV haeIII fnu4HI asuI bbvI CGGCGC AGTGCTGCAA | | pst[M.Hl-] fnu4HI bbvI sfaNI TTGCTGCAGG CATCGTGGTG | alui GTTAGCTCCT CAATCGAGGA | fokI sf CATCCTAAG GTAGCCATTC | th fn GGATAATACC CCTATTATGG |
| ATCT | sau96I avaII asuI GGTCCTGCAA | | Caaaaaagcg GTTTTTCGC | nlaiii ACTGICATGC TGACAGTACG | gai AII[M.hpaII YI I hindII hincII CGTCAACACG |
| ACGATACGGG AGGGCTTACC TGCTATGCCC TCCCGAATGG | haeIII sau961[M.haeIII-] asuI hinPI aeIII-] hhaI GGGCCGA GCGCAGAAGT | GTTGTTGCCA | am-] nlaIII CCATGTIGTG | TAATTCTCTT | ms hp sor nci cau TCTTGCCC |
| | [K.h GAA CTT | hinPI hhai msti fspi TTTGCGCAAC | sau3AI mboI[dam- dpnI alwI nlaIII ACATGATCCC CCZ TGTACTAGGG GGG | fnu4HT bbvI G CAGCACTGCA | ACCGAGITGC TGGCTCAACG |
| GIAGATAACT CATCTATTGA | | bsrI mseI AGTAGTTCGC CAGTTAATAG TCATCAAGCG GTCAATTATC | AI [dam-] AAGGCGAGTT TTCCGCTCAA | I GTTATG | fnu4HI GTATGCGCC CATACGCCGC |
| ii ifi TCCCCGTCGT AGGGGCAGCA | : AGCAATAAAC : TCGTTATTTG | | sau3AI mbol[dam dpnI CCCAACGAIC AAG | GTTATCACT | ddel CAAGTCATTC TGAGAATAGT GTTCAGTAAG ACTCTTATCA |
| plei hinfi GTIGCCIGAC TO | . CAGATTTATC GTCTAAATAG | alui AGCTAGAGTA TCGATCTCAT | mspi hpali alui nlaiv AGCTCCGGIT TCGAGGCCAA | fnu4HI haeIII eaeI fGCCGCAGT ACCGCGTCA | d CAAGTCATTC GTTCAGTAAG |
| foki I TICATCCATA AAGTAGGTAT | mspI hpaII hphI nlaIV I TCACGGCTC AGTGGCCGAG | scrFI ncil mspI hpaII caulI GTTGCGGGA | . GGCTTCATTC CCGAAGTAAG | AGAAGIAAGI TCTTCATTCA | rsal scal AGTACTCAAC TCATGAGTTG |
| 4001 | 4101 | 1201 | 4301 | 4401. | TITUTE QUEE |

| *** | | | au96I aeIII sul sul nli AGG | | | |
|--|---|---|---|---|----------|---|
| hgiai bsp1286 apali CG TGCACCCAAC | CGGAAATGIT GCCTTTACAA | AAAATAACA TTTTATTGT | sau96I haeIII asuI ecol! mnlI TATCACGAGG | | | |
| AACCCACT TIGGGIGA | AAGGGCGACA TTCCCGCTGT | TGTATTTAGA ACATAAATCT | AAAATAGGCG TITTATCGCC | | | 97 3387 |
| rI Idam-] tagI AGTICGAIGT TCAAGCIACA | AAAAGGGAAT TTTTCCCTTA | CATATTTGAA GTATAAACTT | msel TTAACCTATA AATTGGATAT | | | 2790 3071 3297 |
| bsri sau3Ai mbol [dam- dpni alwi xhoIi bstXI GTTGAGATCC AGT | fnu4HI AATGCCGCAA TTACGGCGTT | nlaIII spHI I CA TGAGCGGATA GT ACTCGCCTAT | nlaiii bsphi TATCATGACA ATAGTACTGT | | | 2571 2771 2 |
| sau3AI mboi[dam-] dpni hoII stYI lwI GA TCTTACCGCT | AGGAAGGCAA TCCTTCCGTT | nlai bsphi bsmai TATTGTCTCA TATARCAGAGT A | AAACCATTAT TTTGGTAATA | | • | 2241 2314 |
| sau37 mbol dpn xholi xboli bstYI alwI CTCTCAAGGA TC | GAGCAAAAAC CTCGTTTTTG | TTATCAGGGT AATAGTCCCA | ahali acyl ddel aatii GACGICTAAG | | | 6 1223 2184 |
| GGGGCGAAAA | hphi GITTCTGGGT CAAAGACCCA | ATTGAAGCAT TAACTTCGTA | AGIGCCACCT TCACGGIGGA | | | 4941 651 734 786 4311 4374 |
| I AACGTTCTTC TTGCAAGAAG | hphi TITCACCAGC AAAGIGGICG | SSPI TTICAATAT AAGTTATAA | aI-] TTCCCCGAAA AAGGGGCTTT | | | 4941 2901 1849 2256 2716 4559 4941 4559[M.hpaII-] 3887 3906 4598 72 203 271 481 3433 3690 4211 |
| xmn TCATTGGAA | dam-] - sfani G CAICTTTTAC C GTAGAAATG | mboli eari ACTCTTCCTT TGAGAAGGAA | hinPI hhai thai fnuDII V bstUI[M.hhaI-] CCGCGCACAT TTCCCCGAAA GGCGCGTGTA AAGGGGCTTT | II TTCAA AAGTT | | 401144600 40444600 4046464646464646464646464 |
| hgial bsp1286 AAAAGTGCTC A | mboil[dam-] sau3AI mboi[dam-] dpni sfaNi TGATCTTCAG CAICTTTAC | GAATACTCAT CTTATGAGTA | nlaiv AATAGGGGTT (TTATCCCCAA (| mboli CCCTTTCGTC TTCAA GGGAAAGCAG AAGTT | th: 5015 | aatii(GACGTC): accii(GTNKAC): acciii(TCCGGA): acyi(GRCGYC): ahaii(GRCGYC): ahaii(TTTAAA): |
| 109 | 4701 | 4801 | 4901 | 5001 |)iength: | aatii accii accii ahaii ahaii |

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125 701 1289 1538
295 587 2779 4090 4855
495 1139 1650 2556 2946 3444 4605 4690
3860 4869 4866
3870 896 1049 1368 1695 1966 1990 2398 2877 2905 3533 3546 3663 4069 4187
4230 4494 4669
501 524 1627 3157 3278 3291
511[M.hhaɪ-] 1203 1419 1429 1574 1600 1722 1819 2191 2292 2668[M.hhaɪ-] 2688[M.hhaɪ-]
5712[M.hhaɪ-] 2730[M.hhaɪ-] 2732[M.hhaɪ-] 2732[M.hhaɪ-] 2730[M.hhaɪ-] 2730[M.hhaɪ-] 3775 2810 3771 3782 3868 3880 4665
50 1099 1399 1629 4411
57 488 546 579 1158 1766 1928 2940 3405 3814 3980 4520 4946
139 851 1095 1340 1646 1853 2254 2720 3697 3772 3783 3791 3869 3881 3986 4327
351 1095 1339 1340 1852 2253 2254 2719 2720 3697 3771 3783 3868 3881 4345 4648
                                                                                                                                                                                                                                                                                     204 207 479 1221 1384 1591 1615 1744 1747 1870 2664 2769 2866 3035 3053 3472
3537 3540 3746 4074 4263 4440
138 .
                                                                                                         4999
                                                                              4194
641 1024 1445 1624 1666 1945 2134 2476 4065 4144 4161 4383
                                                                                                                                      641 1024 1624[dcm-] 1666 1945 4161 4383
                                                                                                                                                                                                                         1339 2253 [M.mspr-] 2719 [M.mspr-]
1474 2522 3971
2556
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90 1199 1629 4411
90 1199
                                       1541
2946 3444 4690
                                                                                                                                                                                              1629 [dcm-]
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           008 4812
                                                                                                                                                                                                                                                                                                                            bclI[dam-](TGATCA):
bglI(GCCNNNNNGGC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      draI(ITTAAA):
draIII(CACNNNGTG):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      earI(CTCTTC):
eco0109I(RGGNCCY):
                                        + (DIOMNNOTO) INSTE
                                                                                                                                                                                                                                                                                                                                                                                                          bsp1286(GDGCHC):
                                                                                                                 aval(CYCGRG):
Avall(GGWCC):
avall(ATGCAT):
Avrll(CCTAGG):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    bstYI(RGATCY);
cauII(CCSGG);
cfrI(YGGCCR);
ddeI(CTNAG);
dpnI(GATC);
                                                                                                                                                                                                                                                                                                                                                                                                                           bspHI(TCATGA):
bspHI(TCCGGA):
                                                         aseI(ATTAAT):
aseI(ATTAAT):
asuI(GGNCC):
                                                                                                                                                                                                                        bamHI (GGATCC):
                                                                                                                                                                                                                                              banI(GGYRCC):
banII(GRGCYC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 ecoRI(GAATTC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   ecoRII (CCWGG):
                                                                                                                                                                                                                                                                                                                                                                   hamI(GAATGC):
                                                                                                                                                                                                                                                                                                                                                                                      hemal(GTCTC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               eael(YGGCCR):
                                                                                                                                                                                              ball(TGGCCA):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        batwi(CCWGG):
batwi(CGCG):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     eagI(CGGCCG):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      ecoR''(GATATC)
   alwI(GGATC):
                                                                                                                                                                                                                                                                                      bb::I(GCAGC):
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201 2664 2686 2700 2769 2866 2919 3035 3053 3056 3174 3329 3472 3537 3540 3746 4064 2686 2700 2769 2866 2919 3035 3053 3056 3174 3329 3472 3537 3540 3746 4074 4263 4413 4440 4535 4764 2011 1203 1419 1429 1574 1600 1722 1819 2191 2292 2668 2688 2712 2730 2732 2835 211 1203 1419 1429 1574 1600 1722 1819 2191 2292 2668 2688 2712 2730 2732 2835 28 811 959 963 1866 1955 2033 2194 2805 4003 4184 4471 26 1629 3143 3154 3606 1955 2033 2194 2805 4003 4184 4471 256 1629 3143 3154 3606 1955 20134 2334 2476 3144 3155 3173 3607 4065 4145 4412 495 1139 1650 2946 3444 4605 4690 4560 1474 2522 3971
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  1443 1469 1670 1850 1997 2257 2587 2717 2776 2810 3337 3484 3510 3700 44205 4315 4557 380 561 575 1492 1713 2494 2740 2749 3874 4101 4497 4723 4738 409 542 1181 1184 1786 2613 3009 3780[dam-] 3871[dam-] 4626 4704[dam-]
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     505 685 901 1489[M.hphi-] 1710[M.hphi-] 2216 2412 2434 3030 3105 3501
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    5009
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   206
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      mboI [dam-](GATC):
                                                                                                                                                                                                                                                                                                                                                                                                                             hincII(GTYRAC):
hindII(GTYRAC):
hindII(AAGCTT)
                                                                                                                                                                                                                                                                                                                               hqijii(GRGCYC)
hhai(GCGC):
                                                                                                                                                                fspi(TGCGCA):
hael(WGGCCW):
haell(RGCGCY):
                                                                                                                                                                                                                                                                    hqal(GACGC):
hgial(GAGCWC):
hgicl(GGYRCC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       hinfi(GA::TC):
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 nael(GCGGG):
ncil(CCSGG):
ndel(CATATG):
nhel(GCTAGC):
                                                    [m::HI (GC::GC)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   hpal(GTTAAC)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              hphI(GGTGA):
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                                                                                                             (DOSO) IIGnuj
                                                                                                                                                                                                                                                                                                                                                                                          hinPI(GCGC):
                                                                                                                                                  for: (GGATG)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       msel(TTAA)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         mspI(CCGG)
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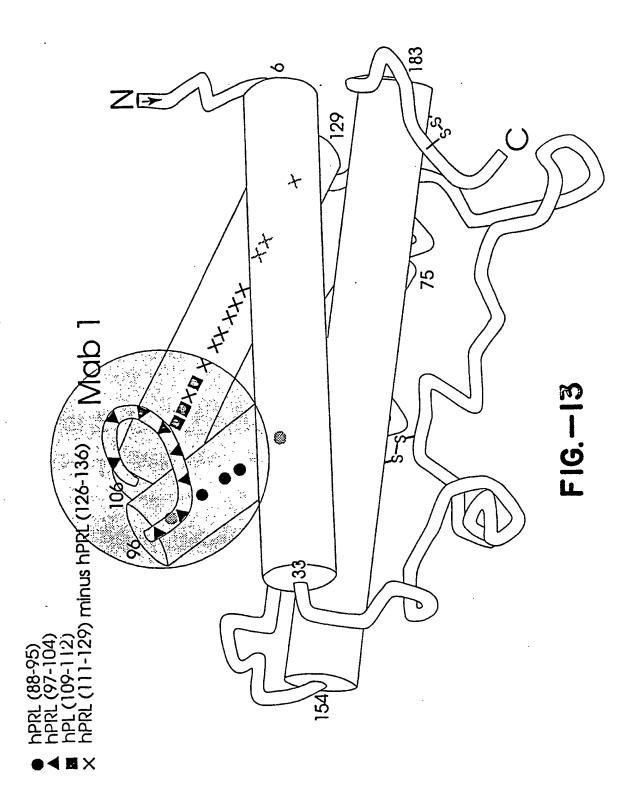
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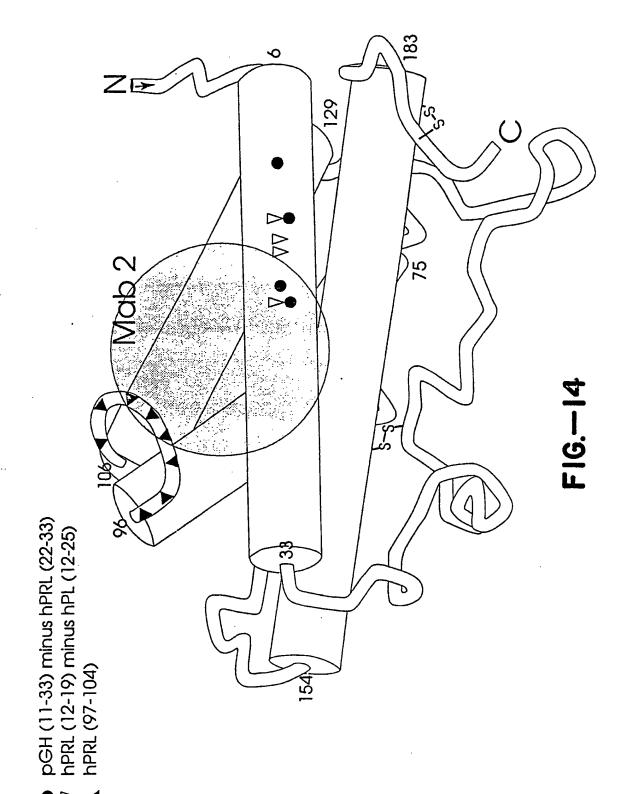
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4342
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501 524 1627 3157 3278 3291
175 237 416 1252 1362 1606 1858 1867 1954 2032 2095 2806 2922 2977 2998 3218
4270 4480 4710
217
338
2275 4825
526 [dcm-]
637 1554
1453 2518 3230 4674
211 1203 1419 1429 1574 1600 1722 1819 2191 2292 2668 2688 2712 2730 2732 2835
2874
2874
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139 851 1095 1340 1646 1853 2254 2720 3697 3772 3783 3791 3869 3881 3986 4327
4345 4391 4649 4666 4702
641 1024 1445[M.haeIII-] 1624[dcm-] 1666 1945 2134[M.haeIII-] 2476[M.haeIII-]
4065[M.haeIII-] 4144[M.haeIII-] 4161 4383 4999[M.haeIII-]
40 597 623 905 1176 1332 1436 1643 1777 2002 2066 2131 2766 2871 3131 3851 4352 4430 4466 4859 4964 550 641 1024 1339 1439 1474 1509 1623 1666 1945 2253 2522 2543 2555 2719 31 3199 3971 4065 4106 4317 4907 1198 1175 2001 2765 3130 14 1500 1549 505 685 2412 2434 3030 3501 4018 640 1623 1665 44065 44018 4264 [M.H1-]
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                                                                                                                                                                                                                                                             270 650 733
                                                                                    noti(GCGCCGC):
nail(ATGCAT):
napcix(RCATGY):
pflai(CCANNNNTGG):
                                                                                                                                                                                                                                                                                                                                                                                            scal(AGTACT):
scrFI(CCSGG):
scrFI[dcm-](CCWGG):
sfawl(GCATC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        " thilli(GACNNNGTC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    xhoIi(RGATCY):
xmaIII(CGGCCG):
xmnI(GAANNNTTC):
                                                                                                                                                                                          ppuMI(RGGWCCY):
prtI(CTGCAG):
pruI(CGATCG):
pvuII(CAGCTG):
                                              nlal" (GGNNCC):
                                                                                                                                                                                                                                                                                                                                                  : (CONCC) :
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     snaBI(TACGTA):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    spel(ACTAGT):
sspl(AATATT):
stul(AGGCCT):
styl(CCWWGG):
tagl(TCGA):
     nlaIII(CATG):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  xbal(TCTAGA):
                                                                                                                                                                        ole1 (GAGTC):
                                                                                                                                                                                                                                                                                                       sau3AI (GATC)
                                                                                                                                                                                                                                                                                   rsal(GIAC)
```

FIG.-12M

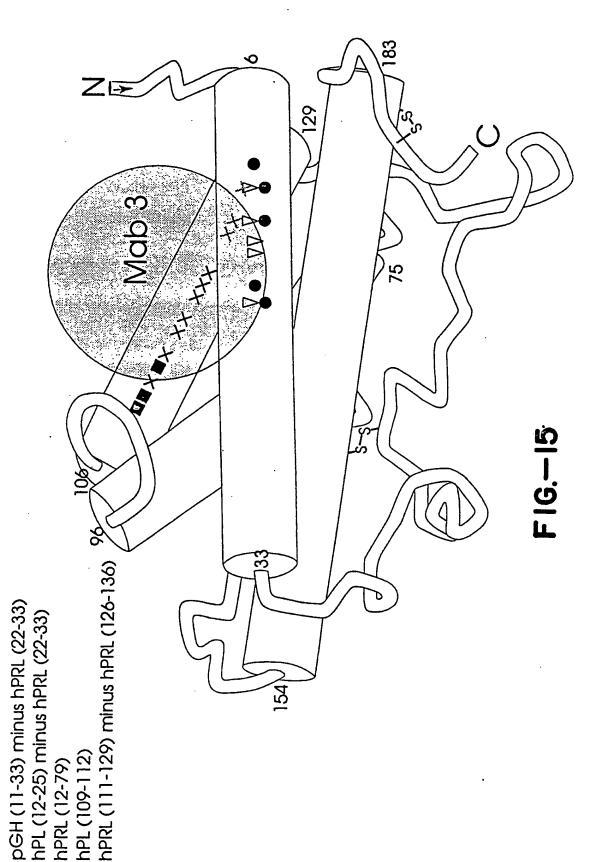
httl(CTTAAG), apal(GGGCCC), asp718(GGTACC), asulf(TCGAA), bgll(AGATCT), bspMI(ACCTGC), bstHI(GCGCGC),
bstBI(TTCGAA), bstEII(GGTNACC), bstXI(CCANNNNNTGG), bsu36I(CTNAGG), clai(ATCGAT), eco8ll(CCTNAGG), ecoNI(CCTNNNNNAGG),
espI(GCTNAGC), kpnI(GGTACC), mluI(ACGCGT), mstII(CCTNAGG), narI(GGCGCC), ncoI(CCATGG), nruI(TCGCGA), paeR7I(CTCGAG),
rsrII(CGGWCCG), sacI(GAGCTC), sacII(CCGCGG), salI(GTCGAC), sfiI(GGCCNNNNNGGCC), smaI(CCCGGG), sphI(GCATGC),



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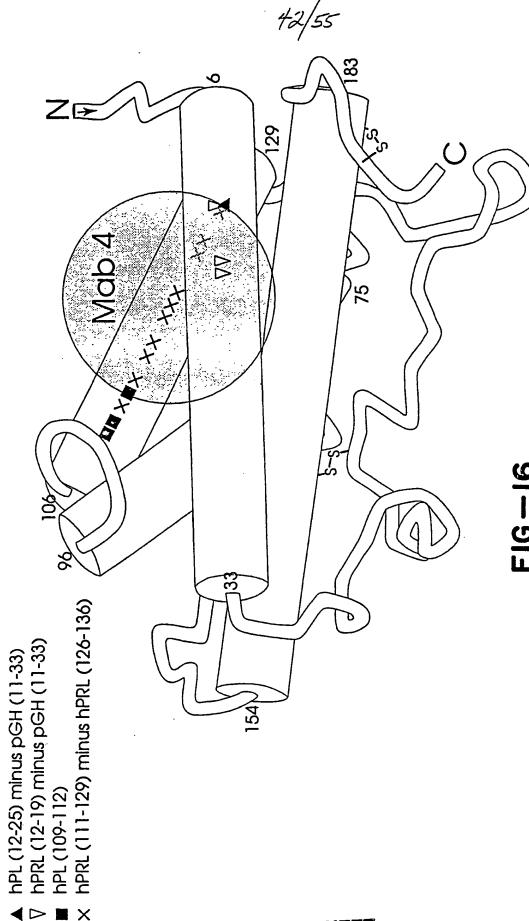


SUBSTITUTE SHEET

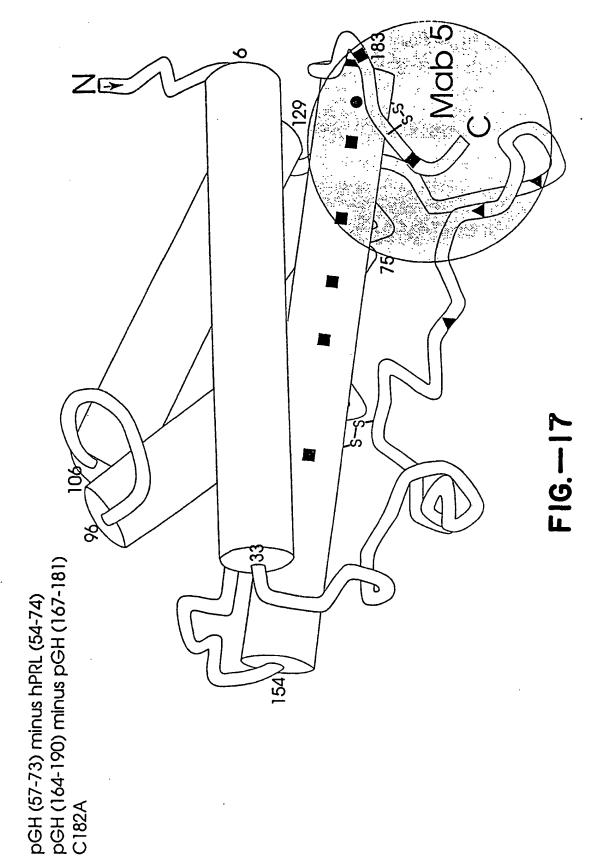


• **∢**▷ **■** ×

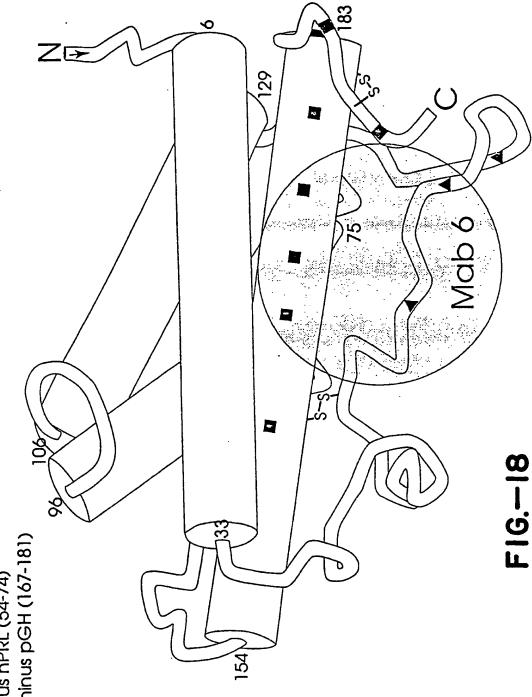
Ł



SUBSTITUTE SHEET

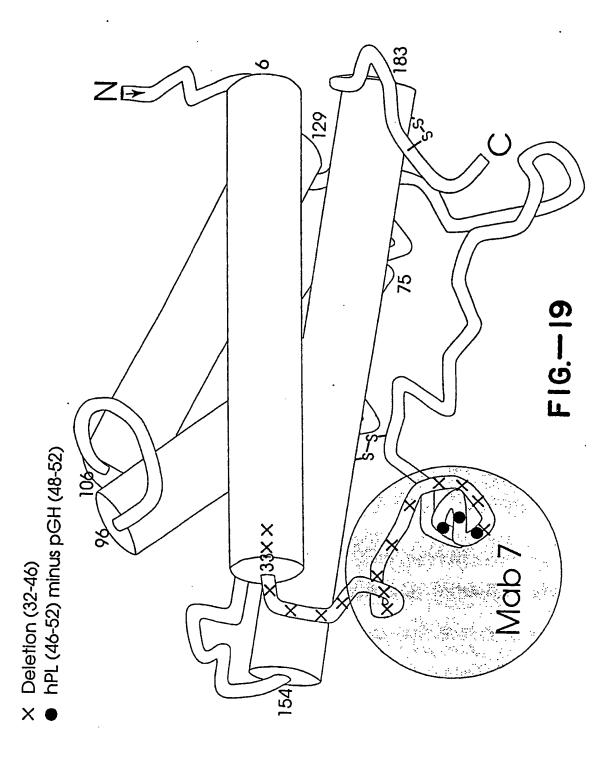


4 m •



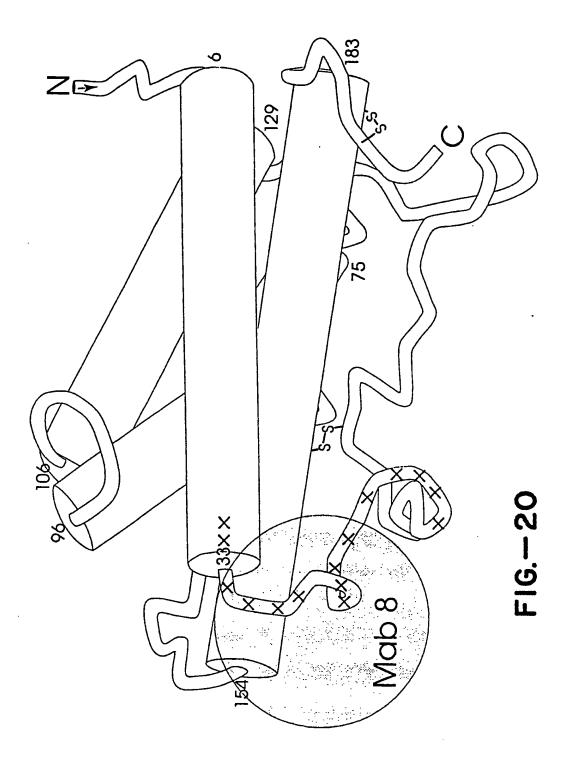
pGH (57-73) minus hPRL (54-74) pGH (164-190) minus pGH (167-181)

4 m



SUBSTITUTE SHEET

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X Deletion (32-46)

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SUBSTITUTE SHEET

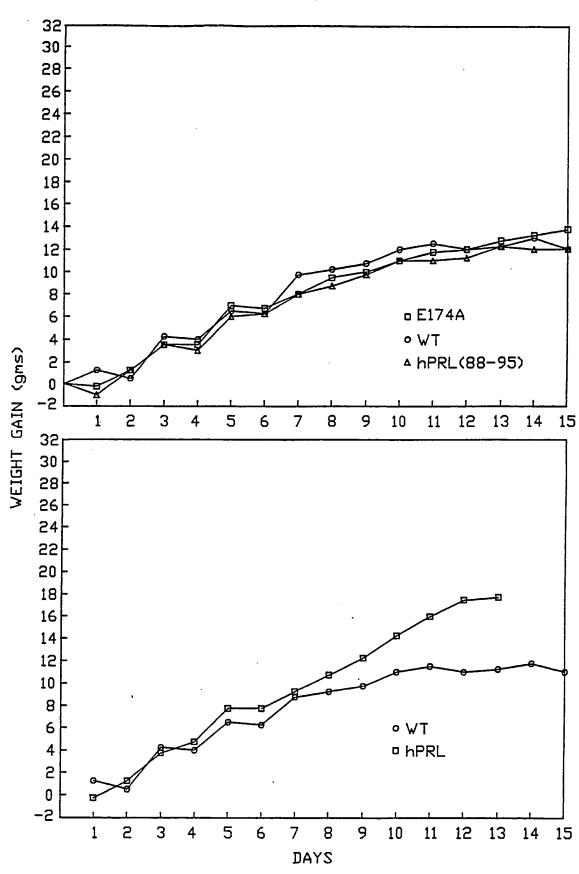
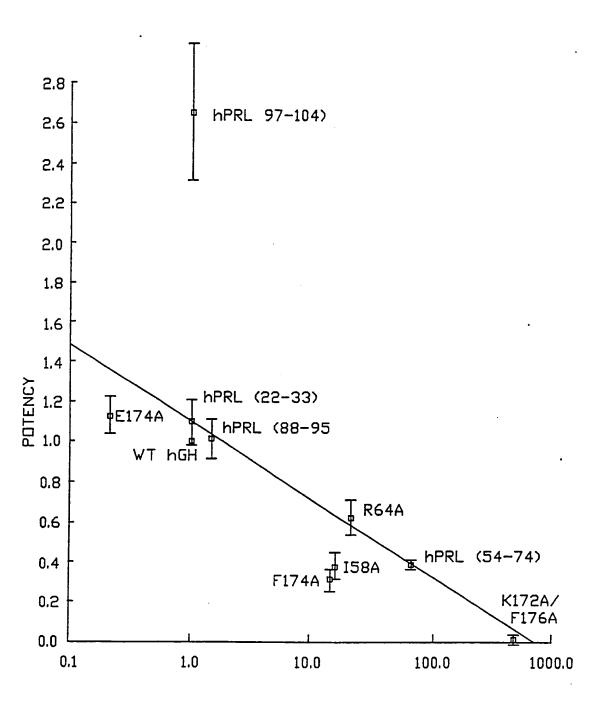


FIG.-22

SUBSTITUTE SHEET

GH ANALOG BIOPOTENCY IN RATS AFTER 8 DAYS OF TREATMENT

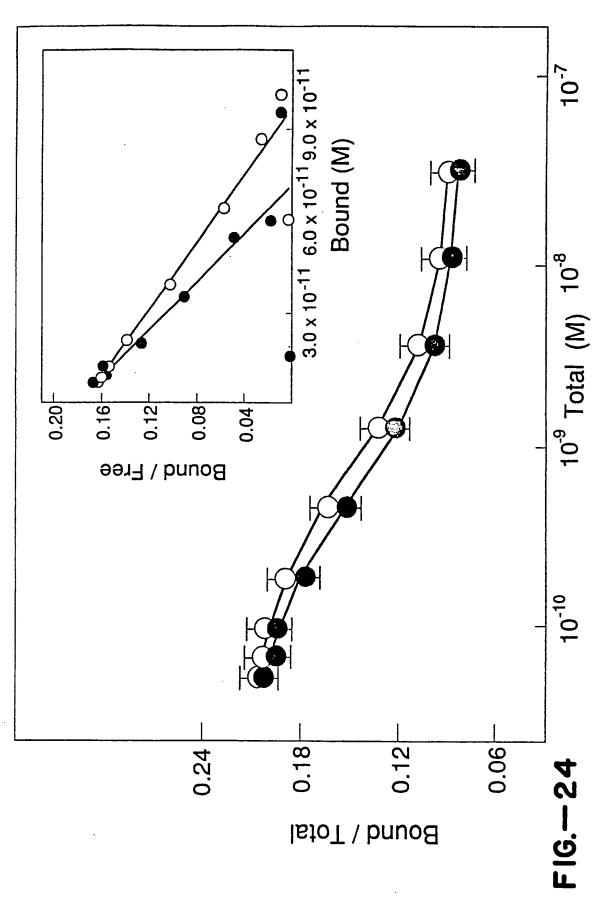


Kd MUTANT/Kd WILD TYPE

FIG. - 23

SUBSTITUTE SHEET





SUBSTITUTE SHEET

Binding Determinants for hGHr

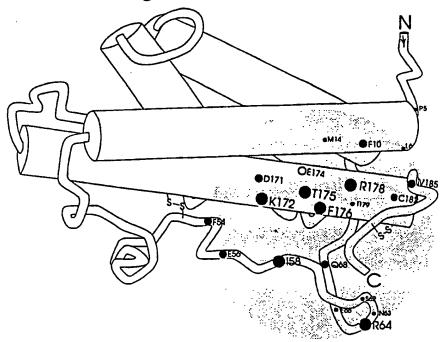
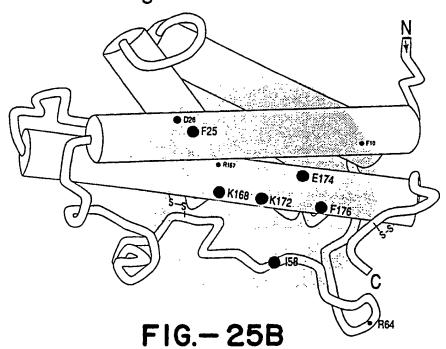


FIG.-25A

Binding Determinants for hPRLr



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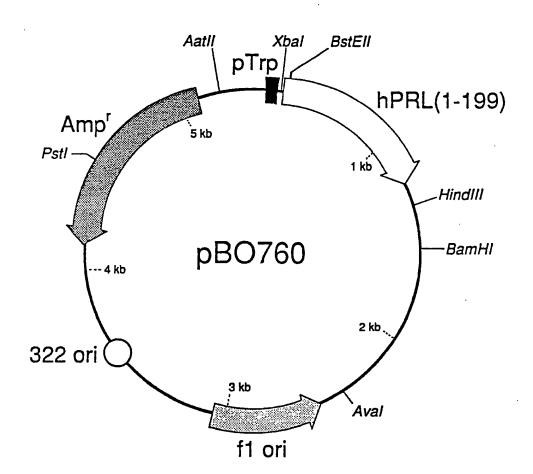
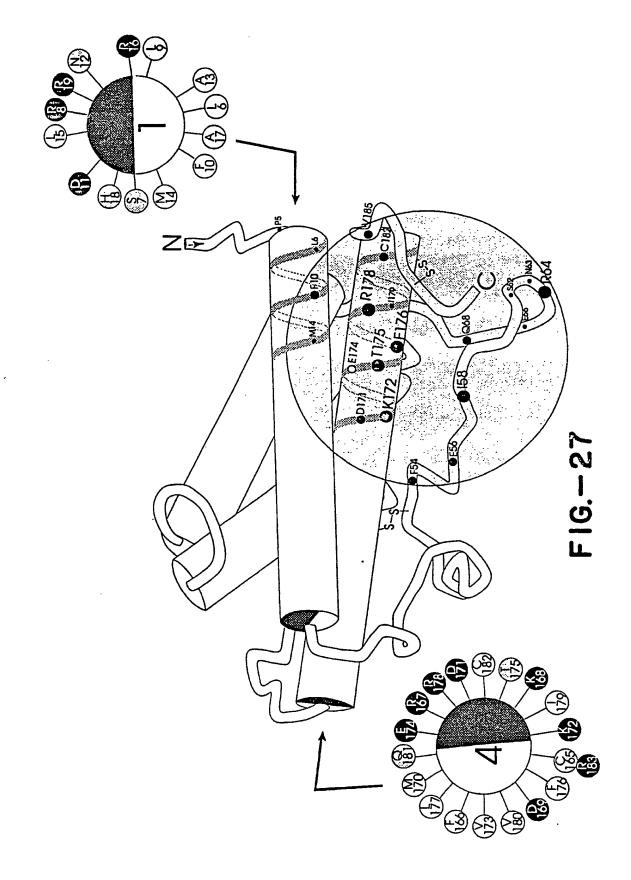


FIG.-26



SUBSTITUTE SHEET

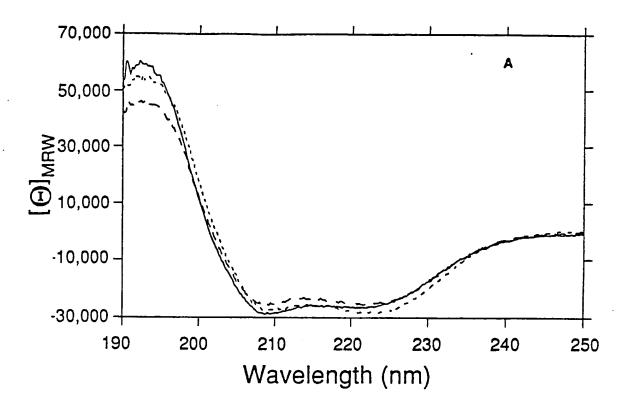


FIG.-28A

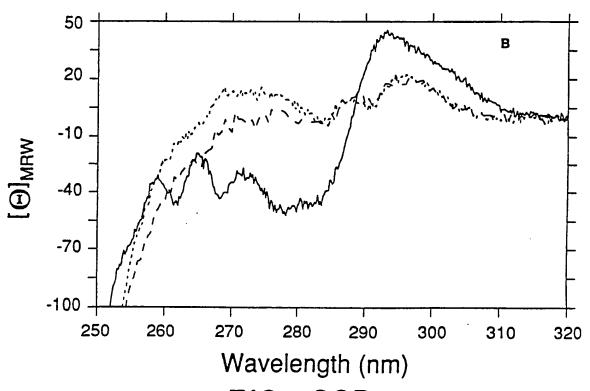
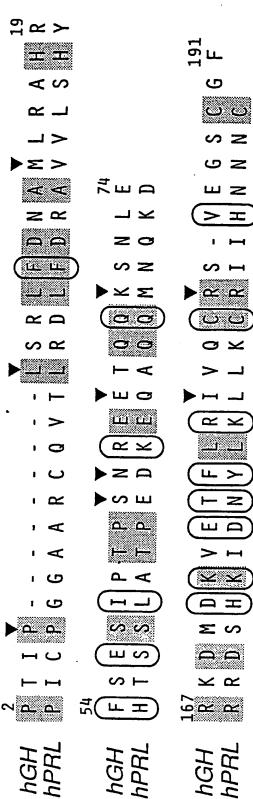


FIG.-28B



-16.-29

'NTERNATIONAL SEARCH REPORT

| | | International Application No. FCT | /0589/04//8 | |
|--|--|---|-----------------------------|--|
| | TON OF SUBJECT MATTER (if several classi | | | |
| According to Inter | national Patent Classification (IPC) or to both Nat | | | |
| IPC (5): | GO1N 33/53,31/00, 33/543, 435/7; 436/501, 504, 518, | | | |
| | | J46 | | |
| II. FIELDS SEAF | | | | |
| | Minimum Documer | | | |
| Classification Syste | m | Classification Symbols | | |
| | | | | |
| U.S. | 435/7; 436/501, 504, | 518, 548; 935/79, | 81 | |
| | Documentation Searched other to the Extent that such Documents | han Minimum Documentation are Included in the Fields Searched 8 | | |
| | | | | |
| | ABSTRACTS SERVICE ONLIN PATENT SYSTEM | NE, BIOSIS PREVIEWS | , | |
| III DOCUMENTS | CONSIDERED TO BE RELEVANT 9 | | | |
| | itation of Document, 11 with indication, where app | ropriate of the relevant passages 12 | Relevant to Claim No. 13 | |
| Category | nation of Ducoment, With indication, where app | opinite, or the relevant passages | | |
| CUI | ience, Volume 244, issu NNINGHAM, B.C., ET AL itope Mapping of hGH-Re Alanine-Scanning Mutag | , "High Resolution ceptor Interactions | 1-13,16-31 | |
| CUI And Ide | Science, Volume 243, issued 1989, CUNNINGHAM, B.C., ET AL, "Receptor and Antibody Epitopes in Human Growth Hormone Identified by Homolog-Scanning Mutagenesis", 1330-1336. | | | |
| is: "Lo on | Biochem. Biophys. Res. Commun., Volume 135, issued 1986, SOUROUTON, M.C., ET AL, "Localization of a Highly Immunogenic Region on the Acetylcholine Receptor Alpha-Subunit", 82-89. | | | |
| | ·• | | | |
| "A" document de | ries of cited documents: 10 afining the general state of the art which is not to be of particular relevance | "T" later document published after the or priority date and not in conflicted to understand the principle invention | ct with the application but | |
| "E" earlier document but published on or after the international "X" document of particular relevance: the claimed invention | | | | |
| filing date cannot be considered novel or cannot be considered to "L" document which may throw doubts on priority claim(s) or involve an inventive step | | | | |
| "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the | | | | |
| | iferring to an oral disclosure, use, exhibition or | document is combined with one | or more other such docu- | |
| other means | • | ments, such combination being of in the art. | bylous to a person skilled | |
| | ublished prior to the international filing date but e priority date claimed | "&" document member of the same p | eatent family | |
| IV. CERTIFICATION | | | | |
| Date of the Actual Completion of the International Search Date of Mailing of this International Search Report | | | | |
| Date of the Words | and the state of t | 05 MAR 1990 | | |
| 02 Februa | ary 1990 | O D MAN 1330 | | |
| International Searching Authority Signature of Authorized Officer | | | | |
| 757/IS | | KAREN I. KRUPEN | | |

| ategory • | Citation of Document, with indication, where appropriate, of the relevant passages | Relevant to Claim No |
|-----------|---|----------------------|
| ategory | Citation of Becomer With Indicates, wind appropriate of the Indicate passages | |
| A | Endocrinol., Volume 121, issued 1987, WERTHER ET AL, "Localization and Characterization of Insulin Receptors in Rat Brain and Pituitary Gland Using In-Vitro Autoradiography and Computerized Densitometry, 1562-1570. | 1-13,16-3 |
| A | Endocrinology, Volume 107, issued 1980 MILLS, T.B. ET AL, "Fragments of human growth hormone produced by digestion with thrombin: chemistry and biological properties", 391-399 (See Ababract, 143544) | 1-13,16-3 |
| A | Chemical Abstracts, Volume 108, no. 11, issued 1988, (Columbus, Ohio, U.S.A) B. C. Cunningham, "Improvement in the alkaline stability of subtilisin using an efficient random mutagenesis and screening procedure", Abstract. | 1-13,16-3 |
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the invention first mentioned in the claims; it is covered by claim numbers: 1-13 and 16-31

4. As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

☐ The additional search fees were accompanied by applicant's protest.
 ☐ No protest accompanied the payment of additional search fees.

Remark on Protest

J

ATTACHMENT TO PCT/ISA/210 Part IV. Before #1, Observations

- I. Claims 1-13 and 16-31 are drawn to a method for identifying unknown active domains in the amino acid sequence of polypeptides classified in class 436, subclass 501.
- II. Claims 14, 15 and 32-64 are drawn to a method of forming a growth hormone variant and the growth hormone variants produced classified in class 530, subclass 350.
- III. Claims 65-79 are drawn to human prolactin hormone variants classified in class 530, subclass 399.
 - IV. Claims 80-83 are drawn to human placental lactogen variants classified in class 530, subclass 399.
 - V. Claims 84-86 are drawn to DNA sequences and expression vectors and hosts classified in class 536, subclass 27.